AR201-13831

The Procter & Gamble Company
Miami Valley Laboratories
11810 E. Miami River Road
Cincinnati, Ohio 45253
www.pg.com

January 8, 2002

Gov. Christine Todd Whitman, Administrator
United States Environmental Protection Agency
PO Box 1473
Merrifield, VA 22116

Attn: Chemical Right-to-Know Program

Dear Governor Whitman:

The Procter & Gamble Company is pleased to provide the enclosed assessment of Nonanoic acid, sulfophenyl ester, sodium salt—CAS RN 91125-43-8 under the HPV Challenge Program. The EPA Tracking Number is 201-01390. P&G understands there will be a 120-day review period and that all comments received by EPA will be forwarded to us for consideration.

This submission includes a paper copy and also an electronic copy on the enclosed diskette.

EPA or other stakeholders may contact me with any questions or concerns at greggs.wj@pg.com or 513-627-1383.

Sincerely,

William J. Greggs
Product Safety and Regulatory Affairs

AR201-13831A

HPV Test Plan and Screening Level Assessment

for

Nonanoic acid, sulfophenyl ester, sodium salt
CAS #: 91125-43-8

Prepared for the HPV Challenge Program by:
The Procter & Gamble Company

December 21, 2001

HPV Test Plan and Screening Level Assessment

Nonanoic acid, sulfophenyl ester, sodium salt
CAS RN: 91125-43-8

Table of Contents

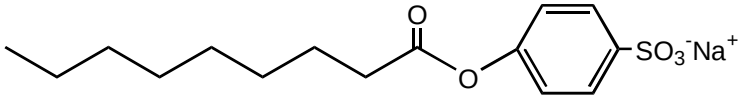
[1] Executive Summary

[1.1] CAS RN: 91125-43-8

[1.2] Substance Name: Nonanoic acid, sulfophenyl ester, sodium salt (Nonanoyloxybenzene sulfonate—NOBS)

[1.3] Structure and Synthesis

(C15 H21 O5 S Na):



NOBS can be made by reacting Nonanoyl chloride (CAS RN 764-85-2) and Sodium phenol sulfonate (CAS RN 1300-51-2). The alkyl chain of NOBS is generally linear and saturated. As the structure diagram shows the sulfonate group is predominately in the para- position. Purity of commercial production ranges from 90-99%.

[1.4] Production Volume

Nonanoic acid, sulfophenyl ester, sodium salt (Nonanoyloxybenzene sulfonate, NOBS) is a proprietary material of The Procter & Gamble Company (P&G). Total tonnage reported in the 1998 IUR was 11,100 metric tons. (1 metric ton = 2204.6 lbs).

[1.5] Use Pattern and Function

The sole use of NOBS is in P&G laundry granular and tablet detergent products intended for household use at a maximum level of 6%. Less than 20% of US granular/tablet laundry detergents contain this ingredient. NOBS is produced as an extrudate and then formulated with other detergent ingredients. P&G has marketed laundry detergent products containing NOBS in the United States for 15 years. Prior to, and since introducing NOBS to the marketplace, P&G has conducted a broad range of hazard and exposure evaluations, both alone and as used in laundry detergent products. In addition, it is estimated that NOBS-containing detergents have been used by more than 100 million consumers in washing more than 12 billion loads of laundry. P&G's extensive post-marketing surveillance and the long history of marketplace experience support the safety profile described in the human and environmental assessments.

NOBS is one of several *n*-alkanoyloxybenzene sulfonates (AOBS) that have been developed as bleach activators for inclusion in laundry detergents to create an oxygen based bleaching system. The materials were developed in response to the need for effective warm water (40-60ºC) bleaching agents to replace direct precursors of hydrogen peroxide that exhibit optimum effectiveness at close to boil temperatures (80-90ºC).

Detergent formulations containing NOBS are designed to help ensure rapid conversion of NOBS to the peroxy compound in the wash water. The peroxy compound is short-lived due to rapid bleaching activity. To be effective in the wash cycle, the peracid precursor must be highly water-soluble, undergo rapid and total perhydrolysis, and produce a peracid bleach with surface activity.

[1.6] Environmental Screening Level Assessment

NOBS is highly water soluble and non-volatile. It is degraded (>99%) during the laundry wash process, and any residual NOBS is then rapidly and completely biodegraded and highly removed during wastewater treatment (> 95% removal). With a log Kow of –0.6, NOBS bioaccumulation potential is extremely low. The environmental fate of NOBS during the main phases of its life-cycle (manufacturing, processing, consumer use) was modeled using E-FAST, a U.S. EPA screening level model. Predicted environmental concentrations (PEC) in surface water range from 0.003 ng /l to 16 μg /l, depending upon the scenario assessed. Environmental monitoring studies have not been performed, as modeled estimates suffice for this material.

Three laboratory acute ecotoxicity studies are available for NOBS – for algae, daphnia, and fish (bluegill). The lowest acute toxicity value is 9.3 mg/l for the algae, *Selenastrum capricornutum* (E*b*C50). EbC50 is the concentration of the test substance that results in a 50% reduction in algal biomass following exposure for a determined period of time, typically 72 or 96 hours. The US EPA recommended assessment factor when acute toxicity test data are available for three different aquatic taxa is 100, in order to account for various uncertainties in the measured data; therefore, the Predicted No Effect Concentration (PNEC) is 93 μg/l based on the available data.

The risk to the aquatic environment is characterized by comparing the Predicted Exposure Concentration (PEC) to the Predicted No Effect Concentration (PNEC). If the concentration in the surface water is less than the no effect concentration, then the potential for adverse effects is low. Integrating all the information currently available, the modeled NOBS PEC at manufacturing and processing sites and in surface waters following consumer use (0.003 ng/l to 16 μg/l) does not exceed the PNEC (93 μg/l). The risk characterization ratios (PEC/PNEC) range from 4.3×10^{-7} to 0.17, where the high-end prediction conservatively assumes that neither hydrolysis nor perhydrolysis occurs following discharge at the manufacturing and processing sites and removal in wastewater treatment is 95% vs 99+% observed in studies. These ratios below 1.0 confirm that the potential for adverse environmental effects from NOBS is very low. As detailed in Section [2.3], degradation products from NOBS are also predicted to have low toxicity, to be removed during wastewater treatment and are not likely to persist in the environment.

[1.7] Human Health Screening Level Assessment

An extensive database of toxicology studies exists on NOBS (alkyl chain C9) and closely related n-alkanoyloxybenzene sulfonates, differing only in carbon chain length including C8, and also a 50:50 mixture of C8 and C10. These studies include both SIDS and beyond-SIDS endpoints, and collectively demonstrate that this material possesses a low order of

toxicity. Acute toxicity studies show that NOBS is not measurably toxic by the oral or dermal routes. Studies indicate this material can be moderately to severely irritating to eyes depending on the concentration of the solution and exposure conditions. Skin irritation was slight or negligible after a four-hour exposure in a variety of dermal studies depending on concentrations tested. Longer or repeated dermal exposures to NOBS may result in increased skin irritation. An assessment of the *in vitro* and *in vivo* genotoxicity potential of NOBS shows no evidence of mutagenic or clastogenic activity. Exposure of dams to doses up to 1,500 mg/kg/day of the bleach activator during pregnancy did not result in embryotoxicity or teratogenic effects in offspring. Similarly, no adverse effects were detected on fertility parameters or reproduction following repeated exposure of up to 1,000 mg/kg/day in males and females prior to mating and during pregnancy.

The potential of NOBS to induce and elicit a skin sensitization response has been investigated using a variety of non-clinical and clinical approaches. Two different animal laboratory methodologies were used, the modified Buehler method using guinea pigs and the local lymph node assay using mice. The four animal studies included in this summary show that NOBS as a raw material has the potential to act as a weak skin sensitizer in the guinea pig although these effects are not consistently replicated in all animal studies. Clinical studies show NOBS is not a skin sensitizer in humans at the concentrations associated with use in product. Numerous studies, which included a total of over 2,000 volunteers who gave informed consent, have been conducted on NOBS and/or laundry detergents containing NOBS, demonstrating that this material can be used in product without the risk of inducing or eliciting skin sensitization reactions in humans. The weight of evidence conclusion that NOBS can be safely used in laundry products at concentrations up to 6% is also supported by peer review. In 1986, both P&G's approach to assessing skin safety for laundry products and also the use of NOBS in laundry detergents were reviewed and approved by a group of 16 international dermatologist experts.

The potential for systemic toxicity and functional alterations resulting from repeated exposure to NOBS was evaluated in subchronic toxicity studies by oral and dermal exposure routes. The results from these studies establish that repeated exposure to NOBS via the oral or dermal route does not result in systemic toxicity or histopathological changes in any of the organs or tissues examined. Studies on the absorption, distribution and excretion of radiolabeled NOBS showed the material was very poorly absorbed upon dermal exposure and rapidly absorbed and eliminated within 72 hours following oral gavage, with no evidence of accumulation in any tissue or organ.

In summary, the toxicological profile of NOBS indicates that the material has a low order of toxicity, based on a variety of acute and sub-chronic studies. The only areas where the potential for adverse effects have been observed have been slight to moderate eye and skin irritation when tested at higher concentrations and/or in repeated exposures, and potential skin sensitization, but only in animal (guinea pig) studies, not in humans.

Exposure Data - Based on the chemistry, rapid perhydrolysis during wash (>99% in 3 minutes), and removability of NOBS during wastewater treatment (>95% of the 1% remaining), there is negligible consumer exposure to this material under recommended use situations. This assessment is based on a thorough attempt to identify the intended and

reasonably foreseeable uses for laundry products containing this material, to assess those resultant exposures, and to evaluate the relevant exposures by way of a high-end analysis. A discussion of this analysis, the methods used for the exposure assessment, and their accuracy and relevance are presented. Where appropriate from a scientific standpoint, related individual exposures are aggregated thus yielding a maximum probable exposure for the chemical.

NOBS is used in household laundry detergents as a bleach activator that results in generation of an oxygen based bleaching system. Based on this use, workers and consumers may be exposed to NOBS although the type of relevant exposure varies for these two populations.

Worker Exposure - For workers, inhalation and dermal exposure to NOBS during the production, formulation or transportation process is limited due to process design that produces a low vapor pressure, non-respirable extrudate (particles of 500 - 1000 μm) as well as industrial hygiene standards and personal protective equipment that are standardly utilitized in production facilities. Employee exposure is minimized through engineering controls and good industrial hygiene practices to ensure exposure is below an OEG of 0.1 mg/m^3. Processing experience with a variety of ingredients in the manufacturing of laundry detergents confirms that these practices are effective in minimizing worker exposure. Worker exposure in commercial and industrial laundries is not expected since these are not intended uses.

Consumer Exposure - Due to the rapid perhydrolysis reaction of the material when formulated in finished product and under use conditions, the potential for consumer exposure to NOBS is very limited. Consumer monitoring studies have not been performed, as modeled estimates suffice for this material. The most relevant and anticipated exposure to consumers is via dermal exposure. Dermal exposure can result from hand laundering of fabric or using a concentrated paste for pretreatment of fabric. Exposure from hand laundering is estimated at 7.5×10^{-6} g/kg/day and exposure from fabric pretreatment is estimated at 4.1×10^{-4} g/kg/day. For these dermal exposures, only 1% is expected to be absorbed based on ADME data. Incidental exposure to unreacted NOBS can occur while scooping the product from the box or from direct exposure to the dry laundry detergent during a spill but both of these exposures would be insignificant by orders of magnitude in comparison to hand laundering or fabric pretreatment. Any residual amount of detergent that may remain on fabric after laundering would not contain NOBS due to the complete perhydrolysis of the material in the wash water. Consumer exposure to the tablet form of the product is expected to be the same as or less than with the granular form.

There is no anticipated oral exposure under recommended use conditions. Due to the complete perhydrolysis, degradation of NOBS and it's removal during waste water treatment, the potential level in drinking water is negligible to nil. Exposure calculations based on estimates of NOBS in drinking water using the EPA's E-FAST model (conservatively assumes perhydrolysis is not complete, some NOBS remains and none is removed in drinking water treatment facilities) resulted in estimated values of 3.9×10^{-8} mg/kg/day. E-FAST provides screening level estimates of concentrations of chemicals

released to the environment from consumer products and is designed to provide high end to bounding estimates of exposure as is appropriate for screening level assessments.

Consumer inhalation exposure during use is limited by a number of factors: the low vapor pressure of NOBS, its production in extrudate form, and the overall design of the laundry product as a non-friable, dense granular or tablet material. Thus, there is very little dust involved in transferring the product from the package to the washing machine so the potential for inhalation exposure from this action is negligible.

Children's Exposure - Exposure of children to NOBS and detergents containing NOBS is expected to be infrequent and negligible based on the recommended use of the product. The product is intended for use by adults and perhaps adolescents in conjunction with automatic washing machines. There may be accidental ingestion of laundry detergents containing NOBS by children however these would be infrequent and result in mild transient symptoms, if any are present, such as nausea, vomiting and/or diarrhea, consistent with the effects observed following accidental ingestion of other laundry products. Any dermal exposures by children should be limited to detergent residues on clothing, which, as discussed above, will not contain any NOBS based on the chemistry and complete perhydrolysis of the material in the wash water.

Summary of human health assessment - The data summarized above demonstrate that NOBS has a favorable safety profile for use in consumer laundry detergents. The risk to human health is characterized by comparing the estimated human exposure to the No Observed Effect Level (NOEL) from animal studies. The amount by which the NOEL exceeds the estimated exposure is referred to as the margin of exposure and this should be sufficiently large to account for several sources of uncertainty and variability in extrapolating data from animal studies to man. Based on the data presented, no adverse effects for humans are expected via any relevant exposure route. The aggregate dermal exposure from hand laundering and pretreatment of fabrics results in an estimated exposure of 4.2×10^{-4} g/kg/day. In comparing this conservative estimate to the results from the dermal subchronic study where the no effect level (NOEL) is greater than 0.4 g/kg/day, the margin of exposure is acceptable. Even at the highest dose tested in this study (2 ml/kg of a 20% test material solution) there were no systemic effects. The only effect noted was irritation at the site of application, which was dose related and limited the amount that could be repeatedly administered. Studies evaluating the dermal absorption of NOBS showed this material is very poorly absorbed through the skin—less than 1%. For potential oral exposure, if one assumes conservatively that perhydrolysis does not occur, that NOBS would be present in drinking water and not removed in drinking water treatment facilities, the calculated exposure using EFAST would be 3.9×10^{-8} mg/kg/day. The NOEL in an oral dietary study was 1.1 g/kg/day. Comparing the estimated oral exposure to the oral NOEL results in a margin of exposure of many orders of magnitude, even after accommodating inter- and intraspecies variation.

[1.8] HPV Test Plan Status

	Data Available	Data Acceptable	Testing Required
Physical/Chemical Characteristics			
Melting Point	Y	Y	N
Boiling Point	Y	Y	N
Vapor Pressure	Y	Y	N
Partition Coefficient	Y	Y	N
Water Solubility	Y	Y	N
ENVIRONMENTAL FATE			
Photodegradation	N	Not relevant	N
Stability in Water	Y	Y	N
Transport (Fugacity)	Y	Y	N
Biodegradation	Y	Y	N
Perhydrolysis	Y	Y	N
Ultimate removability	Y	Y	N
ECOTOXICITY			
Acute Toxicity to Fish	Y	Y	N
Acute Toxicity to Invertebrates	Y	Y	N
Acute Toxicity to Aquatic Plants	Y	Y	N
MAMMALIAN TOXICITY			
Acute Toxicity	Y	Y	N
Genetic Toxicity-Ames	Y	Y	N
Genetic Toxicity-Chromosomal Ab.	Y	Y	N
Unscheduled DNA Synthesis	Y	Y	N
Repeated Dose Toxicity	Y	Y	N
Developmental Toxicity	Y	Y	N
Reproductive Toxicity	Y	Y	N
Eye Irritation	Y	Y	N
Skin Irritation	Y	Y	N
Dermal Sensitization	Y	Y	N
ADME	Y	Y	N

[1.9] Sponsor's Conclusions and Recommendation

The available data on NOBS hazard and exposure demonstrates that there is negligible likelihood of harm to man and the environment during manufacture and use of this material in laundry detergents. All SIDS and other relevant endpoints are complete with reliable data, showing that the material possesses a low order of toxicity. NOBS is a P&G proprietary material and hence the production volume and use pattern are under strict control. Aquatic PEC/PNEC ratios range from 4.3×10^{-7} to 0.17. Exposure to NOBS in the workplace is limited due to a process design that produces a low vapor pressure, non-respirable extrudate. Employee exposure is further minimized through engineering controls and good industrial hygiene practices to ensure exposure is below an OEG of 0.1 mg/m^3. Consumer evaluations indicate that margins of exposure are acceptable and calculations supporting these estimates are conservative. Considering the completeness, accuracy, and relevance of both the hazard and exposure evaluations, NOBS is recommended as sufficiently studied and a low priority for further work.

[2] Environmental Assessment

[2.1] Introduction

NOBS is a proprietary bleach activator exclusively used in granular and tablet laundry detergents intended for household use. For the present assessment, the total tonnage of NOBS is thus assumed to be released down-the-drain. Each of the reports obtained was reviewed to determine adequacy according to U.S. EPA criteria and reliability per Klimisch *et al.* (1997). Robust summaries were prepared for each report with the highest Klimisch scores according to the guidelines recommended by the U.S. EPA (U.S. EPA, 1999) for each study type. These methods include consideration of the reliability, relevance and adequacy of the data in evaluating their usefulness for hazard assessment purposes. The codification described by Klimisch specifies four categories of reliability for describing data adequacy. These are:

> 1—Reliable without Restriction: Includes studies or data complying with Good Laboratory Practice (GLP) procedures, or with valid and/or internationally accepted testing guidelines, or in which the test parameters are documented and comparable to these guidelines.
> 2—Reliable with Restrictions: Includes studies or data in which test parameters are documented but vary slightly from testing guidelines.
> 3—Not Reliable: Includes studies or data in which there are interferences, or that use non-relevant organisms or exposure routes, or which were carried out using unacceptable methods, or where documentation is insufficient.
> 4—Not Assignable: Includes studies or data in which insufficient detail is reported to assign a rating, e.g., listed in abstracts or secondary literature.

Robust study summaries for endpoints with available and reliable data for NOBS are provided in Appendix A and are summarized in Tables 1 to 3.

Table 1: Physical/Chemical Property Data

PHYSICALCHEMICAL	RESULTS	Unit	PROTOCOL
Melting Point [a]	> 360	°C	Metal block method, EEC Directive 67/548. Klimisch 1
Boiling Point [a]	> 360	°C	Metal block method, EEC Directive 67/548. Not tested
MW	336	(g/mol)	
Relative Density	$D^{20}_4 = 1.236$		Pycnometer method, EEC Directive 67/548. Klimisch 1
Vapor Pressure	1.71×10^{-7}	Pa at 25°C	Vacuum micro-balance method, EEC Directive 67/548. Klimisch 1
Partition Coefficient	- 0.572	Log P_{ow}	HPLC, EEC Directive 67/548. Klimisch 1
Water Solubility	245 ± 8	g/l at 20 °C	Flask stirring method, EEC Directive 67/548. Klimisch 1
Particle size	500 - 1000	µm	Dry Sieve Analysis, CIPAC 1995 Klimisch 1

[a] Melting and boiling point estimates are irrelevant—NOBS decomposes before it melts

Table 2: Environmental fate and pathway data

ENVIRONMENTAL FATE AND PATHWAY	RESULTS	PROTOCOL
Hydrolysis	27 % at pH 6.4 at 20°C after 192 h	FI/MS/MS; "Official Journal of the European Communities" (N°L383A - A6/Water solubility). Klimisch 1
Transport and Distribution between Environmental Compartments	Air: 2.5 x 10^{-18} % Water: 99.9% Sediment: 0.13% Soil: 3 x 10^{-10} %	Calculated Fugacity Level III Type (local exposure, EQC model, Mackay et al, 1996) Klimisch 2
Perhydrolysis	> 99% degradation in the wash after 3 minutes	HPLC; "Official Journal of the European Communities" (N°L383A - A6/Water solubility)
Biodegradation	Theoretical CO_2: 87% after 28 days	Ready biodegradability, OECD 301B. Klimisch 1
Ultimate removability	99.7 ± 2.0 % removal	SCAS test, OECD 302A. Klimisch 1
Photodegradation	Not completed.	Study not relevant— material has low volatility, is degraded in the wash; residual rapidly and completely biodegraded and highly removed during wastewater treatment

Table 3: Environmental toxicity data

ECOTOXICITY	SPECIES	RESULTS	PROTOCOL
Acute Toxicity to Fish	*Lepomis macrochirus* (bluegill)	LC_{50} (96 hr) = 32 mg/l	EPA-660/3-75-009. Klimisch 2
Toxicity to Aquatic Plants (Algae)	*Selenastrum capricornutum*	72 h EbC50 = 9.3 mg/l 72 h ErC50 = 26 mg/l	OECD Guideline 201. Klimisch 1
Acute Toxicity to Aquatic Invertebrates	*Daphnia magna*	48 h EC50 > 1000 mg/l	EPA-660/3-75-009. Klimisch 2

[2.2] Fugacity modeling

Fugacity modeling was performed to estimate transport and distribution into environmental compartments. Given the very low volatility of NOBS, which implies it will not partition to the atmospheric compartment, the question of atmospheric photodegradation is not relevant from a hazard assessment standpoint. NOBS is a highly water soluble and non-volatile chemical. As a consequence, the main environmental compartment to be exposed to NOBS is the aquatic one, as shown by the fugacity model results. The EQC Model (version 1.0.1; Mackay *et a*l.,1996) was used with the chemical input parameters shown in Table 1 and 100% of NOBS released to water in order to model adequately its actual use. NOBS is readily biodegradable. US EPA recommends using half-lives of 5 days for water and soil and 20 days for sediment when predicting the environmental fate of readily biodegradable chemicals (http://www.epa.gov/opptintr/exposure/docs/halflife.htm#eqc). EQC model results are shown in Table 2. EQC predicted that 99.9% of NOBS released to the

environment is distributed to surface waters. Therefore, surface waters should be addressed in risk assessment as the relevant environmental repository.

[2.3] Environmental Fate

NOBS is degraded during the wash process, any residual NOBS is then rapidly and completely biodegraded and highly removed during wastewater treatment (Table 2). Thus, release to the aquatic environment is minimal and no additional studies are suggested for environmental fate endpoints (e.g. Photodegradation). Considering (1) the limited fraction of NOBS released to the environment after use (see below [2.3.3], degradation in the wash solution), and (2) the very low log Pow (Table 1), it is expected that the chemical will not bioaccumulate or be transferred to higher trophic levels or humans via the food chain.

Environmental safety profile of NOBS degradation products

The major degradation products of NOBS (perhydrolysis - major pathway, Appendix B) in the wash solution are pernonanoic acid and phenol sulfonate. Their environmental fate and toxicity profiles are summarized below.

Environmental fate of NOBS degradation products According QSAR (SRC Biowin v3.67) output, probability of linear biodegradability of pernonanoic acid is 0.77; non linear biodegradability probability is 0.92. Probability of linear biodegradability of phenol sulfonate is 0.56; non linear biodegradability probability is 0.60. These high probabilities of biodegradation indicate that the major degradation products of NOBS will also be removed during wastewater treatment and are not likely to persist in the environment.

Environmental toxicity of NOBS degradation products According to QSAR (ECOSAR v0.99e) output, the predicted aquatic toxicity of pernonanoic acid and phenol sulfonate are:

Pernonanoic acid
SMILES : CCCCCCCCC(=O)OO. MOL FOR: C9 H18 O3. MOL WT : 174

ECOSAR Class	Organism	Duration	End Pt	mg/L
Neutral Organic	Fish	14-day	LC50	1738
Peroxy Acids	Fish	96-hr	LC50	0.21
Peroxy Acids	Daphnid	48-hr	LC50	18

Phenol sulfonate
SMILES : Oc1(ccc(S(=O)(=O)(O))cc1). MOL FOR: C6 H6 O4 S1. MOL WT : 174

ECOSAR Class	Organism	Duration	End Pt	mg/L
Neutral Organic SAR	Fish	14-day	LC50	1738
Phenols-acid	Fish	96-hr	LC50	1057
Phenols-acid	Daphnid	48-hr	LC50	240
Phenols-acid	Green Algae	96-hr	EC50	6637

According to QSAR modeling, phenol sulfonate toxicity is low and its contribution to the overall environmental risk is negligible. In contrast, one predicted LC50 value of peracids is low. However, over 90% of the pernonanoic acid bleach is consumed during the first 8 minutes of the wash cycle (based on consumer data of average soil load in a wash and timed trials). Moreover, any pernonanoic acid that survives the wash will react with components in wastewater. The resulting carboxylate will degrade very quickly. Therefore, the environmental safety profile of NOBS degradation products formed during the wash is judged to be favorable.

[2.3.1] Predicted removal of NOBS in waste water treatment plants

Considering the rapid and complete biodegradability and high removal (> 99%) in a semi-continuous activated sludge test, removal in waste water treatment plants is predicted to be greater than 95%. This applies to the less than 1% fraction of NOBS released to municipal wastewater handling and treatment following consumer use and destruction of NOBS during washing (see degradation of NOBS, Appendix B).

[2.3.2] Ecosystem Exposures Related to Emissions from the Production, Handling, or Formulation of the Chemical in Industrial Facilities

The NOBS manufacturing process is enclosed and operates as a controlled release process on a continuous basis, up to 24 h/d, 335 d/y. In the processing plants, NOBS is formulated with other chemicals for ultimate use in granular and tablet detergents. The formulation process includes continuous production, dedicated equipment systems, where no releases occur during regular production. For equipment clean-up, hot water is used and disposed via the drain. Washed-away NOBS, if any, will be rapidly biodegraded and removed in the sewer and publicly owned treatment works connected to the processing plants. The Environmental fate of NOBS (surface water concentrations at the point of discharge for low flow, i.e., 7Q10) at the manufacturing and the production sites was modeled with E-FAST, a U.S. EPA screening model, using the “general population exposure from industrial releases” option. The assumptions used in this assessment approach included: 335 days of operation, 11,100 tonnes production, 0.15 % loss from equipment cleaning (e.g., wash down of the tower, scrubber water) and from spillage (U.S. EPA 1996), all the aqueous release goes to municipal waste water treatment before release to the environment. NOBS is manufactured at the Eastman Chemicals plant in Batesville, Arkansas (Table 4). 7Q10 represents the lowest flow for 7 consecutive days in a 10-year period and represents a high end to bounding estimate of dilution of the plant effluent.

Table 4: Details of NOBS manufacturing site (Batesville plant), according to E-FAST

FACILITY NAME: EASTMAN CHEMICAL CO		
FACILITY LOCATION: BATESVILLE AR72501		
RECEIVING WATER NAME: WHITE R		
REACH NUMBER: 11010004001	FACILITY ON REACH: No	DICHARGE TYPE: Indirect
NPDES PERMIT #: AR0035386	DATA SOURCE: FacSrch	

Integrating processed NOBS tonnage, loss rate from equipment cleaning and from spillage in plants, removal in waste water treatment plants, and number of processing days, the post-treatment discharges to the wastewater treatment plant at the Eastman Chemical plant was 2.5 kg NOBS/d, causing a predicted aquatic exposure concentration of 16 μg NOBS/l.

NOBS is incorporated into detergent formulas at the two following plants of the Procter & Gamble Company: Augusta - POTW NPDES # GA0020087 (Table 5) and Alexandria/Pineville - POTW NPDES # LA0033464 (Table 6). Fifty-five % of NOBS produced in the Eastman plant (i.e., 6,100 metric tons/y) is formulated in the Alexandria/Pineville plant, 45% (i.e., 5,000 metric tons/y) in the Augusta plant.

Table 5: Details of NOBS processing site (Augusta plant), according to E-FAST

FACILITY NAME: AUGUSTA WPCP		
FACILITY LOCATION: AUGUSTAGA30911		
RECEIVING WATER NAME: SAVANNAH R		
REACH NUMBER: 03060106045	FACILITY ON REACH: No	DICHARGE TYPE: Indirect
NPDES PERMIT #: GA0020087	DATA SOURCE: FacSrch	

Integrating processed NOBS tonnage, loss rate from equipment cleaning and from spillage in plants (0.15%), removal in waste waster treatment plants, and number of processing days (250 d/y), the post-treatment discharges to the wastewater treatment plant at the Augusta plant was 1.1 kg NOBS/d. The 7Q10 surface water concentration for the 10^{th} %tile low flow was 0.23 μg/l.

Table 6: Details of NOBS processing site (Pineville plant), according to E-FAST

FACILITY NAME: PINEVILLE CITY OF		
FACILITY LOCATION: PINEVILLLA71360		
RECEIVING STREAM NAME: RED R		
REACH NUMBER: 08040301020	FACILITY ON REACH: Yes	DISCHARGE TYPE: Direct
NPDES PERMIT #: LA0033464	DATA SOURCE: FacSrch	STATION ID: 07355500

Integrating processed NOBS tonnage, loss rate from equipment cleaning and from spillage in plants (0.15%), removal in waste waster treatment plants, and number of processing

days, the post-treatment discharge to wastewater treatment at the Pineville plant was 1.4 kg NOBS/d. The 7Q10 surface water concentration for the 10^{th} %tile low flow was 0.38 μg/l.

[2.3.3] Ecosystem Exposures Related to the Use and Disposal of Products Containing NOBS

NOBS enters the public domain in the form of household laundry products intended for disposal to sewer. The chemistry of NOBS during the wash (see degradation of NOBS in Appendix B) indicates that little, if any NOBS enters the environment under expected consumer use and disposal patterns. The detergent formulations containing NOBS are designed to help ensure rapid conversion in the wash water of NOBS to the peroxy compound. NOBS is short-lived (< 1% remaining after 3 minutes in wash) due to the instability of the peroxide (O-O) bond. To be effective, the bleach activator NOBS must be highly dispersed in water, undergo rapid perhydrolysis, and produce a fatty peracid bleach with some degree of surface activity. NOBS fulfills these requirements in the presence of bleach, e.g., sodium percarbonate or sodium perborate, in the laundry detergent product. Due to the presence of excess sodium percarbonate or sodium perborate in the product, the bleach activator molecule reacts quantitatively, within one minute, in an aqueous detergent solution to form primarily the peracid bleach (perhydrolysis). Phenol sulfonate is the other perhydrolysis product. The bleach activator molecule is designed so that the ester perhydrolysis, the preferred reaction, dominates over straightforward hydrolysis or diacyl peroxide formation.

[2.3.3.1] Reactions occurring in the wash solution

NOBS is stable in neutral (pH 7) solution but it readily degrades in acid (pH<6) and alkaline (pH>8) solutions, e.g., in the wash solution. A full discussion on NOBS perhydrolysis is reported in Appendix B. Perhydrolysis is the desired and favored reaction under wash conditions. Under the temperature and pH conditions created by the detergent formula in the wash solution, sodium perborate monohydrate releases hydrogen peroxide that reacts with NOBS to form the peroxy acid, pernonanoic acid, and at the same time releases phenol sulfonate. These reactions are completed within the first few minutes of the wash. The measured degradation of NOBS at 40°C in a 1% aqueous detergent solution was extremely fast: after 3 minutes, NOBS could no longer be detected. The reactions are somewhat slower in cold-water wash conditions but still completed within the wash cycle.

[2.3.3.2] Consumer Product Releases Influent Concentration

The concentration of NOBS in the influent of municipal wastewater treatment plants was estimated using E-FAST's Down-the-Drain scenario. We assumed per capita water use of 364 l/cap.day, a US population of 2.5×10^8 (EPA defaults), 99% degradation of 11,100 tonnes during the wash (see [2.3.3.3]), and no loss of NOBS in the sewage collection and conveyance system. Assuming a removal of 95% during waste water treatment, the 10th percentile low flow PEC was 0.04 ng NOBS/l and the 50th percentile low flow PEC was 0.003 ng NOBS/L.

[2.3.3.3] Summary of Predicted Surface Water Concentrations

Source	Predicted surface water concentrations
Manufacturing site (Batesville plant)	16 μg NOBS/l
Processing site (Augusta plant)	0.23 μg NOBS /l (7Q10, 10th %tile low flow)
Processing site (Pineville plant)	0.38 μg NOBS /l: (7Q10, 10th %tile low flow)
Consumer Product Use	0.003 ng NOBS/l(50th %) to 0.04 ng NOBS/l(10th %)

Environmental monitoring studies have not been performed, as modeled estimates suffice for this material.

[2.3.3.4] Other Sources of Ecological Exposure

There are no additional ecological exposure sources of NOBS (e.g. no non-chain of commerce or natural sources).

[2.4] Ecotoxicity

Three laboratory acute ecotoxicity studies are available for NOBS – for algae, daphnia, and fish (bluegill). The lowest acute toxicity value was 9.3 mg/l for the algae, *Selenastrum capricornutum* (E*b*C50). The US EPA assessment factor when acute toxicity test data are available for three different aquatic taxa is 100; therefore, the Predicted No Effect Concentration, PNEC, or Concentration of Concern, is 93 μg/l based on the available data. Although the fish and daphnia tests were conducted before GLP implementation in toxicity laboratories (1982), QSAR (ECOSAR, SRC Program) results confirmed that algae (predicted EC50 = 44 mg/l) were more sensitive to NOBS than fish (predicted LC50 = 560 mg/l) and daphnia (predicted LC50 = 3280 mg/l).

[2.4.1] Algal Growth Inhibition test

The acute E*b*C50 value was 9.3 mg/l for the algae, *Selenastrum capricornutum*. This test was supported by analytical confirmation of exposure concentrations. The geometric mean of the measured concentrations was calculated.

[2.4.2] Acute Fish test

The acute LC50 value was 32 mg/l for the fish, *Lepomis macrochirus*. The test was not supported by analytical confirmation of exposure concentrations. The dissolved oxygen levels dropped below 20% saturation after 48 h. It is at that time that mortality occurred. The reported fish mortality was mainly the result of stress due to low oxygen level. In addition, the stability test data (Robust summary 3.1.2) indicate NOBS to be stable in water, at neutral pH, for 96h.

[2.4.2] Acute Daphnia test

The acute LC50 value was greater than 1000 mg/l for *Daphnia magna*. The test was not supported by analytical confirmation of exposure concentrations.

[2.5] Environmental Screening Level Assessment

The risk to the aquatic environment is characterized by comparing the predicted exposure concentration (PEC) to the concentration of concern (CoC or PNEC). If the concentration in the surface water is less than the concentration of concern, then the potential for adverse effects is low. Integrating all the information currently available, NOBS PEC, at manufacturing and processing sites and in surface waters following consumer use, never exceeds the concentration of concern (93 μg/L). These assessments conservatively assume that neither hydrolysis nor perhydrolysis occurs following discharge at the manufacturing and processing sites and removal in wastewater treatment is 95% vs 99+% observed in studies. The table below presents the risk characterization ratio (PEC/PNEC) for each life-cycle stage of NOBS, i.e., from manufacturing to consumer use. The ratios below 1.0 confirm that the potential for environmental adverse effects from NOBS is very low. Degradation products from NOBS are also predicted to have low toxicity, be removed during wastewater treatment and not likely to persist in the environment.

Life-cycle stage	**PEC**	**PNEC**	**PEC/PNEC**
Manufacturing (Batesville)	16 μg NOBS/l	93 μg NOBS/l	0.17
Processing (Augusta)	0.23 μg NOBS /l		2.5×10^{-3}
Processing (Pineville)	0.38 μg NOBS /l		4.1×10^{-3}
Consumer Product Use	0.04 ng NOBS/l		4.3×10^{-7}

[2.6] References

Klimisch *et al.* (1997) Reg Tox Pharm 25: 1-5

Mackay D, DiGuardo A, Paterson S, Cowan CE (1996) Environ Tox Chem 15: 1627-1637

U.S. EPA (1996) Chemical Evaluation Branch (CEB) 8/16/1996. Generic Scenario: Surfactants in Industrial and Commercial Laundries. US EPA, Washington, DC

Draft guidance on developing robust summaries. http://www.epa.gov/chemrtk/robsumgd.htm

[3.0] Human Health Assessment

[3.1] Introduction

NOBS is a proprietary bleach activator exclusively used in granular and tablet laundry detergents. Each of the reports obtained was reviewed to determine adequacy according to EPA criteria and reliability per Klimisch *et al.* (1997). Robust summaries were prepared for each report with the highest Klimisch scores according to the guidelines recommended by the EPA (U.S. EPA, 1999) for each study type. Robust study summaries for SIDS endpoints, as well as several relevant endpoints beyond SIDS, with available and reliable (according to Klimisch criteria) data for NOBS are provided in Appendix A and are summarized in Table 7.

Table 7 Summary of SIDS Endpoints

Acute Mammalian Toxicity			
Acute Oral Toxicity	Rats	Oral gavage. 10 rats/group. Doses 5.10, 5.78, 6.46, and 7.14 g test material/kg body weight of 40%w/v suspension in distilled water.	Acute oral LD_{50} = 6.03 g/kg Klimisch 1
Acute Dermal Toxicity	Rabbits	24 hour exposure to 2 ml/kg of a 40% w/v aqueous solution on intact (3 rabbits) or abraded (3 rabbits) skin.	Acute dermal LD_{50} > 2.0 ml/kg (0.8 g/kg) Klimisch 1
Mutagenicity/Genotoxicity			
Ames Assay	Salmonella and E. coli strains	Plate incorporation method. Doses ranged from 50 to 7,000 µl/plate in the definitive study with and without S9 activation.	No evidence of mutagenicity. Klimisch 1
In vivo Chromosomal Aberration Assay	Rats	Acute and repeat dosing regimens used with doses ranging from 0.16 to 3.2 g/kg test material. Positive and negative controls also included.	The test compound has no clastogenic potential under the conditions of this test. Klimisch 1
In vivo Unscheduled DNA Synthesis Assay	Rats	Test material administered at 500, 1000, or 2000 mg/kg bw. Positive and negative controls included. Hepatocytes were harvested and evaluated.	Test article did not induce a significant increase in DNA synthesis. Klimisch 1
Developmental and Reproductive Toxicity			
Developmental Toxicity Study	Rats	Four dose groups 0, 500, 1000, or 1500 mg/kg/day by gavage on gestation days 6-15.	NOEL pup: 1500 mg/kg NOAEL dam: 500 mg/kg LOAEL dam: 1000 mg/kg Klimisch 1
Reproductive Toxicity Study	Rats	Comparable to one generation fertility study. Four dose groups 0, 100, 500, 1000 mg/kg/day by gavage.	NOEL repro: 1000 mg/kg NOAEL systemic: 100mg/kg Klimisch 1
Repeat Dose (Subchronic) Toxicity			
91 Day Oral Toxicity Study	Rats	Dietary levels of 0, 0.001, 0.01 and 0.1% (equivalent to 0, 10, 100, or 1000 mg/kg/day).	NOAEL: 0.11% in diet (approximately 1,100 mg/kg/day) Klimisch 1

Summary of Beyond SIDS Endpoints

Irritation/Corrosivity			
Eye Irritation	Rabbits	LVET method using neat material. No rinse (6 rabbits) and rinse (3 rabbits) conditions.	Slight to moderate irritation, some with corneal involvement, cleared by Day 7 (rinsed) or Day 14 (unrinsed). Klimisch 1
Eye Irritation	Rabbits	FHSA method using neat material without a rinse (3 rabbits), with a rinse (3 rabbits) or with a 10% w/v solution without a rinse (3 rabbits).	Mild to moderate irritation, some with corneal involvement. For the neat material, all irritation cleared within 4 days. For 10% solution, most effects reversible in 4 days and all effects reversible within 21 days Klimisch 1
Skin Irritation	Rabbits	Department of Transportation method. N=6 for 40% w/v suspension and N=6 for undiluted material	40% suspension was slight irritant and neat material was non-irritating. Klimisch 1
Skin Sensitization			
Skin Sensitization	Guinea Pigs	Modified Buehler. Induction dosed at 20% (occluded), challenge at 20%.	No evidence of skin sensitization under the conditions of this test. Klimisch 1
Skin Sensitization	Guinea Pigs	Modified Buehler. Induction dosed at 5.0% (occluded), challenge at 2.5%, rechallenge at 1%	Evidence of skin sensitization under the conditions of this test. Klimisch 1
Skin Sensitization	Guinea Pigs	Modified Buehler. Induction dosed at 10% (occluded), challenge at 0.5%.	No evidence of skin sensitization under the conditions of this test. Klimisch 1
Skin Sensitization	Mice	Local Lymph Node Assay 10%, 5%, 1%, 0.5%	No increase in lymph node cell proliferation and no evidence of skin sensitization under the conditions of this test. Klimisch 1
Repeat Dose (Subchronic) Toxicity			
28 Day Dermal Toxicity Study	Rabbits	0, 1.5% or 20% test material in water (2 ml/kg) dosed on abraded skin for 7 hours/day, 5 days/week for 4 weeks.	NOAEL: 2 ml/kg of 20% solution (0.4 g/kg) - no systemic toxicity. Effects limited to dose related dermal irritation at application test site. Klimisch 1

3.2 Hazard Assessment

The following toxicology data are provided in support of the use of NOBS as an ingredient in laundry detergents. A summary of each study is presented below. Additional information on these studies, including methods, is provided in Appendix A. Studies were conducted on NOBS (C9 AOBS), and in some cases on C8 AOBS, or C8/10 AOBS during the technical research and development of this bleach activator. Approximately 80% of the studies were conducted using the C9 AOBS material, 10% using the C8 AOBS material and 10% using a 50:50 blend of C8/C10 AOBS. These three test materials are identical in structure with the exception of the length of the alkyl chain. Based on published literature and unpublished P&G data, this difference in length of the carbon chain (C8, C9, and C10) is not expected to significantly effect the toxicity profile.

SIDS Endpoints

[3.2.1] Acute Oral Toxicity in Rats (C9 AOBS)

An acute oral LD_{50} toxicity study was conducted on NOBS. A single dose of the test material was administered as a 40% w/v aqueous solution to Sprague-Dawley rats by oral gavage. Test doses were 5.10, 5.78, 6.46 and 7.14 g test material/kg body weight. All animals (10 rats/group; 5 male, 5 female) were observed for mortality and clinical signs at 0.5, 1, 2, 3, and 4 hours after dosing and daily thereafter for 14 days.

The oral LD_{50} for male and female rats (combined Probit method) was calculated to be 6.03 g/kg body weight (95% confidence limits: 5.62 - 6.44 g / kg). All resulting mortality occurred within two days following administration of the test material. Clinical signs observed included diarrhea, abdominal gripping, hypoactivity and decreased respiratory rate. Generally, the signs and number of animals involved appeared to be dose related. All animals that died during the study had irritation or hemorrhaging of the stomach and intestine. All signs are consistent with surfactant related irritation of the GI tract. Necropsy results on surviving animals were unremarkable.

[3.2.2] Acute Dermal Toxicity in the Rabbit (C9 AOBS)

The acute percutaneous toxicity of NOBS was investigated in rabbits. A 40% w/v aqueous solution of the test material was applied to the skin (either abraded or intact) of the shoulder and rump of each rabbit at a dose of 2 ml/kg body weight and covered. Prior to treatment, hair was clipped from shoulder to rump. The skin of group I animals (3 rabbits) was left intact and the skin of group II animals (3 rabbits) was abraded with the clipper head. Test material was spread evenly over the clipped area and immediately covered with 8-ply gauze held in place by a dental dam covering the entire trunk. At the end of the 24-hour exposure period, dressings were removed and the treated area of the skin gently wiped to remove residual material.

Animals were observed for mortality and clinical signs at least once within 4 hours of dosing and daily thereafter for 14 days. If present, clinical signs and deaths were recorded at each observation time. The treated areas of skin were examined 30 minutes after removal of the test material, and then daily thereafter, for signs of dermal irritation. Dermal effects were assessed according to a pre-defined grading scale for erythema, edema and eschar. All animals were necropsied either upon death during the study or at the end of the 14 day observation period.

One animal from the abraded group died on Day 7 of non-treatment related causes (gastro-enteritis of unknown etiology). During the first 6 days following test material administration, dermal irritation ranged from slight to severe erythema, slight to moderate edema and slight atonia. Only slight erythema was observed beyond day 7. All animals had normal weight gain. Except for the local skin effects observed at the site of application, no treatment related gross effects were observed at necropsy. Based on the results of this study, the dermal LD_{50} of NOBS is greater than 2.0 ml/kg (greater than 0.8 g/kg).

[3.2.3] Mutagenicity (C9 AOBS) - Escherichia coli WP2 and WP2 uvrA Reverse Mutation Assay and Salmonella/Mammalian - Microsome Mutagenesis Assay (Ames Test)

The mutagenicity potential of NOBS was evaluated in the bacterial reverse mutation assay using the Escherichia coli WP2 and WP2 uvrA Reverse Mutation Assay and Salmonella/Mammalian-Microsome Mutagenesis Assay (Ames Test) using strains TA1535, TA100, TA1537, TA1538, and TA98. Test material concentrations ranged from 50-20,000 µl/plate in the preliminary toxicity dose range-finding studies and typically 50 to 7,000 µ l/plate in the definitive studies. Appropriate positive, solvent and sterility controls were used. Tester strain titers were determined. All dose levels of test material, solvent and positive controls were plated in triplicate. Following an approximate 48 hour incubation at 37°C, revertant colonies per plate were counted; for all replicate plating, mean revertant colonies were calculated. The results of the E. coli and salmonella/mammalian microsome reverse mutation assays indicate that under the condition of these studies, the test material did not show any evidence of mutagenic potential in any of the tester strains in the presence or absence of Arochlor-induced rat S9 liver microsomes.

Appropriate positive controls indicate a valid test. Both strains TA 100 (base-pair substitution) and TA 98 (frameshift) responded positively to 4-nitroquinoline-1-oxide and strain TA 100 also responded to N-methyl-N'-nitro-N-nitrosoguanidine. The activation systems were tested by positive responses to benzo[a]pyrene and 2-acetylaminofluorene.

[3.2.4] Structural Chromosomal Aberration (C8/10 AOBS)

The objective of this study was to evaluate the clastogenic potential of C8/10 AOBS as manifested by the production of chromosomal abnormalities such as deletions, exchanges, rings and breaks in bone marrow cells of treated rats.

Distilled water and methylmethane sulfonate served as the negative and positive control, respectively, in this study. Rats were dosed by gavage with 3.2 g/kg, 1.1 g/kg, or 0.32 g/kg in the acute dosing regimen phase and sacrificed at 6, 24, or 48 hours post dose while rats in the subchronic regimen received 1.6 g/kg, 0.5 g/kg, or 0.16 g/kg once a day for 5 days. Each dose group and sacrifice time consisted of 3 males and 3 females.

An i.p. injection of colchicine was given to inhibit mitosis approximately 2 hours prior to sacrifice. Bone marrow was collected, fixed, stained and analyzed for chromosomal abnormalities.

The appropriate positive and negative controls indicate a valid test. The results of this study indicate that C8/10 AOBS, administered orally over the dose range of 0.32 - 3.2 g/kg for the acute study and 0.16 - 1.6 g/kg for the subchronic study, did not induce a statistical increase in the number of chromosomal aberrations. Thus the compound has no clastogenic potential under the conditions of this test.

[3.2.5] *In vivo* Unscheduled DNA Synthesis (NOBS extrudate: 78% C9 AOBS)

The potential of NOBS to induce unscheduled DNA synthesis (UDS) in primary cultures of hepatocytes obtained from test article treated rats was assessed. In the *in vivo* UDS study, test and control articles were administered to male rats at a constant volume of 10 ml/kg body weight by a singe gavage injection. Sterile distilled water was selected as the vehicle for the test article. In the UDS assay, male rats were exposed to test article at 0.5, 1.0 and 2.0 g/kg body weight or to vehicle or positive control. No mortality was observed in any test article treated or vehicle control treated rats.

Treatment with NOBS did not induce a significant increase in the mean number of net nuclear grain counts (i.e., an increase of at least 5 counts over the negative control group) in hepatocytes isolated either 2 to 4 hours or 12 to 16 hours after dose administration. NOBS was concluded to be negative in the UDS test with mammalian liver cells *in vivo*.

[3.2.6] Teratology (C8/10 AOBS)

A study was conducted to determine the teratogenic potential of C8/10 AOBS in rats when dosed during organogenesis. Charles River CD rats received the test material once daily by gavage on gestation day 6 through 15, at one of the following doses: 0, 500, 1000, or 1,500 mg/kg/day. Each dose group consisted of 25 presumed pregnant female rats. Maternal body weights and food consumption were recorded on study day 0, 6, 9, 12, 16 and 20. Cesarean sections were performed on all surviving females on gestation day 20. Fetuses were individually weighed, sexed and examined for external malformations and variations. Approximately one half of the fetuses were placed in Bouin's solution for subsequent soft tissues examination using Wilson's sectioning technique. The remaining fetuses were prepared and stained with Alizarin Red S for skeletal examination.

No mortality was present over the course of the study in the control, 500, or 1000 mg/kg/day groups. Three rats dosed with 1500 mg/kg/day died on gestation 13 or 15. Necropsy observations of animals that died on study included reddened stomach mucosa and distended intestines. Clinical observations present in the mid and surviving high dose groups included respiratory rales and wet matted haircoat or material in the facial, ventral and/or anogenital regions. There were no meaningful differences in the gross necrospy of treated and control dams.

Oral administration of C8/10 AOBS from gestation day 6 through 15 resulted in a depression in maternal body weight change at all dosage levels during the first two measured intervals of treatment (days 6 to 9 and 9 to 12) and only in the high dose group during the last treatment interval (days 12 to 16). Mean food consumption was slightly decreased in the mid and high dose groups only during the treatment period.

There were no indications of a treatment related effect on fetal or embryonic growth or survival. Ovulation, implantation, intrauterine development, and embryogenesis were uniform in all study groups. Similarly, the occurrence of external, soft tissue and skeletal malformations and developmental variations was not different in the treated groups relative to the control group. When administered orally to pregnant Charles River CD rats, C8/10 AOBS did not induce a teratogenic effect at dosage levels of 500, 1000, or 1500 mg/kg/day.

The fetal NOEL was determined to be 1500 mg/kg/day and the maternal NOAEL was 500 mg/kg/day.

[3.2.7] Reproductive Toxicity (C9 AOBS)

A study was conducted to evaluate the potential for effects on reproduction and fertility in Sprague Dawley rats following repeated exposure to NOBS. Doses of 0, 100, 500, or 1000 mg/kg/day of NOBS in deionized water (dosing volume of 5ml/kg) was administered by oral gavage for 70 days prior to initiation of mating until termination which occurred on either gestation day 13 or lactation day 21. Each dose group consisted of 38 rats/sex. The F1 offspring were potentially exposed in utero and/or as neonates during lactation via maternal milk but did not directly receive the test article.

The estrous cycle was determined in females 10 days prior to mating until the end of the mating period. Body weights and food consumption were recorded weekly until copulation, on gestation days (GD) 0, 7, 13, and 20 and lactation days 0, 7, 14, and 21 for appropriate groups. Animals were observed daily for clinical signs of toxicity, changes in appearance, behavior and mortality.
In the uterine exam group (on GD13), the ovaries and uterine horns were examined for number of copora lutea, number of implantations, number and distribution of viable and nonviable fetuses, and early resorptions. For the dams that were allowed to deliver, litter size, number of still births, number of live births, and gross anomalies were determined. On postnatal day 4, litters were culled to 10 pups to achieve homogenous group size for evaluation of nursing, survival and body weight. Pups were weighed on postnatal day 0, 4, 7, 14, and 21. Tissues and organs from all F0 animals were macroscopically observed, with special attention to reproductive organs, and preserved in 10% neutral buffered formalin for potential microscopic evaluation.

There was no treatment related difference in the estrous cycle of female rats. Mortality occurred in 1, 1, 2, and 10 rats in the 0, 100, 500, and 1000 mg/kg day groups, respectively. Macroscopic observations noted in three females that died on study included gastric lesions with thickened tissue indicative of gastric irritation. Five males that died in the high dose group had pulmonary lesions suggestive of pneumonia. Test article was not directly implicated in the deaths. Clinical observations in the mid and high dose groups included excessive salivation and respiratory rales. There were no significant adverse effects on body weights or food consumption. The high dose males showed a slight yet consistent decrease in body weights (4% or less decrease) compared to control animals throughout the study. Uterine exam observations show no difference in the number of viable embryos, postimplantation loss, total implantations or number of corpora lutea. For the F0 delivery and F1 litter observations there was no test article effect observed on male or female fertility indices, copulatory indices, gestation length, mean number of live/dead pups on day 0, pup survival to weaning or pup body weight throughout lactation. There were no indications of a treatment related effect on fetal or embryonic growth or survival. Ovulation, implantation, intrauterine development, and embryogenesis were uniform in all study groups.

In conclusion, NOBS administered orally at dosage levels of 100, 500, or 1000 mg/kg/day did not result in adverse effects on fertility, parturition, neonatal viability, growth of the newborn or reproductive performance in rats.

[3.2.8] Subchronic (90 day) Feeding Study (C8 AOBS)

A subchronic feeding study was conducted to assess the potential for systemic toxicity after repeated exposure to C8 AOBS, a material closely related in structure to NOBS (two materials differ only in the length of the carbon chain, C8 vs C9). C8 AOBS was administered in diet daily for 13 weeks to 4 groups of Sprague Dawley rats (40 rats per group, 20 male and 20 female) at levels of 0, 0.001, 0.01 and 0.1% w/w, which equates to approximately 0, 10, 100, and 1000 mg/kg/day. Diets were prepared weekly and evaluated for homogeneity, stability, and dietary concentration of the test material. The concentrations were adjusted each week on the basis of a predicted mid week body weight and an estimate of food consumption for the week in question to provide a constant dose level in relation to body weight (mg/kg/day).

Animals were observed daily for overt signs of toxicity and mortality with detailed clinical examination at weekly intervals. Body weight and food consumption were recorded weekly throughout the study. Clinical chemistry evaluations were performed on blood and urine collected from 10 male and 10 female animals per group during week 12 and 13, respectively, and included hematology, blood chemistry and urinalysis. Opthalmoscopic examinations were performed on all animals in the control and high dose groups prior to the start of treatment, and during week 12.

Complete necropsies were performed on surviving animals at the end of the study. The following tissues were weighed and fixed: adrenals, heart, pituitary, brain, kidney, spleen, testes/ovaries, liver and thyroid. With the exception of the eyes which were fixed in Davidson's solutions, an extensive list of tissues were preserved in 10% neutral buffered formalin as noted in the protocol and Appendix A. All tissues from control and high dose animals, lung and liver tissue and gross lesions from low and intermediate dose groups were embedded in paraffin wax BP, sectioned at a nominal thickness of 5 microns and stained with haemtoxylin and eosin and evaluated by the pathologist.

Administration of C8 AOBS via the diet for 13 weeks did not result in any mortalities or induce any compound-related clinical signs of toxicity. There were no significant changes in body weights, food consumption, opthalmoscopy, clinical chemistry, urinalysis, absolute or relative organ weights or effects in the macroscopic and microscopic pathology.

Increases were observed between the control and high dose group males for neutrophils, lymphocytes, and BUN levels. In addition, creatinine and sodium were different for females. However, these changes were within the normal ranges observed in historical data compiled at the testing laboratory.

No toxicological significant treatment-related lesions were observed. The study established 0.11% in diet (approximately 1,110 mg/kg/day) as the no observed adverse effect level

(NOAEL) and AOBS was considered to be not systemically toxic to the rat up to a level of 1,100 mg/kg body weight/day.

Beyond SIDS Endpoints

[3.2.9] Primary Eye Irritation in the Rabbit (Low Volume Eye Irritation Procedure) (C9 AOBS)

NOBS was evaluated for the potential to cause eye irritation in the rabbit using the Low Volume Eye Test (LVET) procedure (ASTM #). Group I New Zealand White Rabbits received 0.01 ml of test material, placed directly on the cornea of one eye without rinsing. Group II rabbits received 0.01 ml of test material directly on the cornea followed by a rinsing procedure. Treatment groups consisted of 3 or 6 rabbits. Eyes were examined for corneal opacity, iritis and conjunctivitis and scored according to the methods of Draize (1959). The results for Group I (unrinsed) yielded a maximum average score of 33.7 (Day 2). Corneal involvement was observed in 6 of 6 animals. All effects observed were reversible (1 animal in 3 days, 1 in 4 days, 3 in 7 days and 1 in 14 days). The results for Group II (rinsed) yielded a maximum average score of 30 (Day 1). Corneal involvement was observed in 1 of 3 animals. Eyes of all animals returned to normal within 3-7 days (2 animals in 3 days and 1 in 7 days). The test substance caused slight to moderate irritation in all eyes that cleared by Day 7, except for one that cleared by Day 14.

[3.2.10] Primary Eye Irritation in the Rabbit (C9 AOBS)

To comply with European regulatory testing requirements, NOBS was tested in a Draize rabbit eye irritation study using New Zealand White Rabbits. Group I animals received 3 mg of test material placed in the conjuctival sac without rinsing. Group II animals received 3 mg of test material in the conjuctival sac followed by rinsing. Group III animals received 0.1 mL of a 10% w/v solution of the NOBS solution in the conjunctival sac without rinsing. Each groups consisted of 3 animals. Eyes were examined for corneal opacity, iritis and conjunctivitis and scored according to the methods of Draize (1959). The eyes were examined for irritation at specific time intervals, up to a maximum of 35 days, following treatment. The results for Group I yielded a maximum average score of 16.7 (Day 1). Corneal involvement was observed in 2 of 3 animals. All observed effects cleared within 4 days (2 animals in 3 days and 1 in 4 days). The results for Group II yielded a maximum average score of 5.3 (Day 1). Corneal involvement was observed in 0 of 3 animals. The mild conjunctival irritation was transient and cleared in 2 days in all subjects. The results for Group III yielded a maximum average score of 28.0 (Day 1). Corneal involvement was observed in 3 of 3 animals. All effects observed were moderate and reversible (2 animals in 4 days and 1 in 21 days). In summary, the test substance caused slight to moderate irritation in all eyes, which cleared by Day 4, except in the 10% w/v unrinsed group, which cleared by Day 21.

[3.2.11] Primary Dermal Irritation in Rabbits (C9 AOBS)

Two primary dermal irritation studies were conducted on NOBS using New Zealand White rabbits. In the first study, a volume of 0.5 mL of test material (40% w/v suspension of

NOBS in distilled water) was applied to a 1 x 1 inch gauze patch and occluded for 4 hours on intact unabraded skin. In the second study, 0.5 g of test material, slightly moistened with 0.9% saline was applied to a 1 x 1 inch gauze patch and occluded for 4 hours on intact, unabraded skin. Each study consisted of 6 rabbits. After 4 hours of exposure, the patches were removed from animals in both studies and the application sites were graded for irritation and corrosion.

The skin in the area of the application site was graded again at the end of 48 hours (44 hours after first reading). A standardized grading scale, ranging from 0 to 4, was used to score erythema, edema, and other skin effects if present including eschar, ulceration and necrosis. The average dermal irritation scores for animals in the first study at 4 hours were 0.54 and 0 for erythema and edema, respectively; whereas, at 48 hours the scores were 1.3 and 0 for erythema and edema, respectively. The calculated primary irritation index (PII, can range from 0-8 with 0 being a non-irritant) was 0.9, which classifies NOBS as a slight irritant. The average dermal irritation scores for animals in the second study at 4 and 48 hours were 0 for erythema and edema. Under the test conditions in the second study, undiluted NOBS was non-irritating and non-corrosive.

Dermal Sensitization

Based on the weight of evidence from all available data, which evaluated the potential of NOBS and laundry products containing NOBS to cause skin sensitization, it is concluded that NOBS can safely be used in products at levels up to at least 6%. Many of the studies included in the weight of evidence assessment are briefly summarized below. The types of studies included are non-clinical animal studies in guinea pigs and mice, clinical studies which use a variety of test methods including human repeat insult patch tests (HRIPTs), extended home use studies, provocative use studies, hand immersion tests, and T-shirt wear tests.

In 1986, P&G's approach to assess skin safety for laundry products was reviewed, critiqued and approved by a group of 16 world-renowned dermatology experts. In addition, this same group also reviewed and supported the finding that the use of NOBS in product at up to 6% was without risk of skin sensitization as had been demonstrated in non-clinical and clinical studies. As part of regulatory filings, authoritative bodies have concurred with the same conclusion. An overview of the numerous clinical studies conducted on the NOBS material alone as well as in product at up to 6% follows the non-clinical data summary.

Non-clinical animal studies

Four studies are summarized below which investigated the potential of NOBS alone to cause skin sensitization under exaggerated concentrations and conditions. Several studies were conducted using the NOBS material as manufacturing processes and starting materials varied during the research phase of the development process. Results from the non-clinical studies suggest NOBS as a raw material has the potential to act as a weak skin sensitizer in the guinea pig, although these effects are not consistently replicated in all animal studies. One reason for the inconsistent results may be related to the concentration of the active NOBS material. The test material in the first two guinea pig studies contained >95%

NOBS whereas the last two studies were conducted on material in the extrudate form used in laundry detergent products—78% C9 AOBS. The study to evaluate sensitization potential in mice resulted in no evidence of skin allergenicity under the conditions of the Local Lymph Node Assay (LLNA).

[3.2.12] Dermal Sensitization in the Guinea Pig (C9 AOBS)

The potential for delayed contact hypersensitivity reactions to NOBS was evaluated in Hartley albino guinea pigs (10 control animals; 20 test animals). Test material was applied as a 20% solution of NOBS (w/v) in water during induction. The induction concentration was selected based on the minimally irritating dose from skin irritation information for a similar compound. A screening study was conducted to determine the highest non-irritating concentration for challenge. Based on the results, a 20% (w/v, 0.4 ml) aqueous solution was used as the challenge concentration. At 24 and 48 hours post challenge, depilated animals were scored for erythema using a 0-3 scale (0= no reaction, ± = slight patchy erythema, 1= slight, but confluent or moderate, patchy erythema, 2= moderate erythema, 3= severe erythema with or without edema). No evidence of sensitization was observed in guinea pigs exposed under the conditions of this study.

[3.2.13] Dermal Sensitization in the Guinea Pig (C9 AOBS)

A second study was conducted using the modified Buehler protocol. The potential for delayed contact hypersensitivity reactions to NOBS was evaluated in Hartley albino guinea pigs (10 control animals; 20 test animals). Test material was applied as a 5% NOBS aqueous solution (w/v, 0.4 ml) under occlusive patch for six hours once per week during induction. The induction concentration was selected based on the irritating dose from the induction range finding study. A separate range finding study was conducted to determine the concentration for challenge. Based on the results, a 2.5% (w/v, 0.3 ml) solution was used as the challenge concentration. Test animals were rechallenged and a naïve control group was dosed with a 1% solution of test material in distilled water for six hours. Skin was graded at 24 and 44 hours after rechallenge, followed by depilation, and another skin grade at 48 hours.

The test sites were graded for skin responses, including erythema and edema, using a standardized scoring scale at 24 and 48 hours following chamber application at induction. During challenge, the test sites were graded through hair at 19 hours and then following depilation at 24 and 48 hours after patch removal. Irritation was noted during induction. At the 48 hr scoring interval following challenge, a dermal score of 1 was noted in 6/20 and 0/10 test and challenge control animals, respectively. All other scores ranged from 0 to ± in all other test and control animals. During the rechallenge phase, 2/20 test animals presented with a score greater than +/- at 24 and/or 48 hours after rechallenge. The two animals that responded positively during rechallenge also reacted in the challenge phase of the study. Under the conditions of this study, the data indicate a contact sensitization response occurred in some of the test animals at the concentrations tested.

[3.2.14] Dermal Sensitization in the Guinea Pig (NOBS extrudate: 78% C9 AOBS)

A recent study was conducted using the modified Buehler protocol and a sample of NOBS as used in end use product. The potential for delayed contact hypersensitivity reactions to NOBS was evaluated in Hartley albino guinea pigs (10 control animals; 20 test animals). Test material was applied as a 10% solution (w/v, 0.3 ml) under occlusive patch for six hours once per week during induction. The induction concentration was selected based on the minimally irritating dose from the induction range finding animals. A range finding study was conducted to determine the highest non-irritating concentration for challenge. Based on the results, a 0.5% (w/v, 0.3 ml) solution was used as the challenge concentration.

The test sites were graded for skin responses, including erythema and edema, using a standardized scoring scale at 24 and 48 hours following chamber application at induction. During challenge, the test sites were graded through hair at 19 hours and then following depilation at 24 and 48 hours after patch removal. Irritation was noted during induction. At the 24 and 48 hr scoring interval, dermal score of 1 was noted in 1/20 and 0/10 test and naïve control animals, respectively. All other scores ranged from 0 to ± in all other test and control animals. Under the conditions of this study, the test material is not considered to be positive for skin sensitization based on EPA and OECD guidelines.

[3.2.15] Dermal Sensitization in the Mouse (NOBS extrudate: 78% C9 AOBS)

A study evaluated the potential of NOBS to be a skin allergen in mice by using the Local Lymph Node Assay (LLNA). The study consisted of 4 dose groups, a vehicle control group (reverse osmosis water) and a naïve control group, each with 5 mice/group. For each treatment group, five mice were treated daily for three consecutive days by direct epicutaneous application of 25 µl of test article to each ear. In addition a vehicle control (reverse osmosis water) and a naïve control (no treatment) were evaluated. Approximately 71 hours after final test application, mice were injected i.v. in the tail vein with tritiated thymidine to label proliferating cells.

Mice were observed immediately prior to and approximately 2-4 hours after dosing for any significant alterations in appearance of the application site. Mice were observed twice daily for general health and mortality. Five hours after injection, lymph nodes were harvested and single cell suspensions prepared and quantitated by liquid scintillation spectrometry.

All animals appeared normal throughout the study. Body weight gain was noted for all treatment animals during the day -1 and day 6 interval. The stimulation indices of lymph nodes were calculated for each treatment group compared to controls. The groups treated with 10%, 5.0%, 1.0% and 0.5% demonstrated stimulation indices of 0.5, 0.6, 0.9, and 0.7, respectively. A stimulation index of 3.0 (three fold increase over controls) would be considered a positive immunological response for sensitization.

Treatment with the test article did not result in an increase in lymph node proliferation compared to controls demonstrating the test material is not a dermal contact allergen under the conditions of this test.

Summary of the human clinical data

The data summarized below show that laundry detergent product containing up to 6% of NOBS is not expected to present a risk of skin sensitization to consumers.

As noted above, in some animal studies NOBS has the potential to cause contact sensitization in animals when tested under exaggerated concentration and exposure conditions. Human sensitization studies on NOBS alone in over 2,499 volunteers who gave informed consent resulted in 1 weak positive response. That person was able to use detergent product containing up to 6% of NOBS for 14 months at home without skin problems and was found negative in a subsequent diagnostic patch test. In addition, none of the volunteers (>2,000) who participated in clinical tests with NOBS-containing product developed contact sensitization. These tests mimicked under exaggerated conditions the typical use of laundry detergent in the US and included product usage in automatic machines but also product usage in laundry hand-wash lasting at least 10 minutes and pre-treatment of fabrics.

Additional clinical studies included several different methodologies and test designs. The studies below all support the conclusion that NOBS can be safely used in laundry products under use and exaggerated use condition without the risk of skin sensitization. The type of studies include:

- Extended home use tests (n=268 volunteers for 3 months with patch test before and after test)
- Extended laundry pretreatment tests (n=87 volunteers used 50% paste of detergent containing 6% NOBS for 8 weeks with patch test before and after test)
- Extended home use pretreatment (n=117 volunteers used 60% paste of detergent containing NOBS for 12 weeks with patch test at end of study)
- Provocative use test for 14 months with patch testing at 7 and 14 months
- Hand immersion test (n=26 volunteers soaked hands for four consecutive days, include diagnostic patch test before and after study)
- T-shirt wear test (n=130 male volunteers with sensitive skin, in hot humid climate wore T shirts laundered in detergent containing NOBS)

[3.2.16] Repeated Dose Dermal Toxicity in Rabbits (C8/10 AOBS)

The purpose of the study was to assess the percutaneous and systemic toxicity of test article when it is repeatedly applied to abraded skin of New Zealand white rabbits over a period of 28 days. The test material for this study was 50% sodium octanoyloxybenzene sulfonate (C8 AOBS) and 50% decanoyloxybenzene sulfonate (C10 AOBS), which differs from NOBS only in the length of the carbon chain (C8 and C10 vs C9).

For 4 weeks, ten animals per group each were exposed for 7 hours/day, 5 days/ week on abraded skin to 2 ml/kg of water, 1.5% or 20% C8/10 AOBS. Each day of dosing the skin was graded and observations for clinical signs of toxicity were made. Body weights were measured once per week and tissues were taken at the end of the study for microscopic evaluations. The weights of the liver and kidneys were measured and the hemogram for each animal was determined.

No animals died and there were no test article related overt signs of toxicity. There were no differences between the controls and test groups with regard to body weight, weight gain, hematology values and absolute or relative organ weight. The most common symptoms reported were soft stools and diarrhea. These were seen across all groups and both sexes and did not appear to be test article related. There were no test article related gross or microscopic changes observed in any tissues examined except skin. Any differences in hematology endpoints were within the normal clinical limits.

Skin responses, both gross and microscopic, increased with the concentration of test article. Slight erythema and desquamation were observed in the 1.5% group. Exposure to 20% C8/10 AOBS caused slight erythema, edema and desquamation and slight to moderate atonia and fissuring. The microscopic evaluation of the skin from this group revealed dermal effects that included inflammation, parakeratosis, acanthosis, hyperkeratosis, and vesiculation.

The application of test material at levels up to 20% to the abraded skin of rabbits did not cause any detectable systemic toxicity. The effects of C8/10 AOBS in rabbits appears to be limited to dermal irritation and microscopic effects localized to the test application site when applied to the skin in a concentration up to 20% w/v and dosed five days per week for four weeks. The degree of irritation appears to be dose-related.

[3.2.17] Absorption, distribution, metabolism, and excretion (ADME) study (C9 AOBS)

Oral and dermal absorption, distribution, excretion (ADE) studies have been performed in rats using uniformly ring-labelled C9 AOBS (approx. 11 mg/kg). The radiochemical purity of the test material was 97%. The dermal ADME study showed there was no significant absorption by this route of exposure. Less than 1% was absorbed with 0.56 $\pm$ 0.18% eliminated from urine, < 0.02% via CO2, and < 0.16% via faeces after 72 hours. Recovery from the skin application site and the cage wash was 99.1 $\pm$ 1.0% and 0.14 $\pm$ 0.06%, respectively. Total recovery was 101.9 $\pm$ 0.7%.

NOBS was rapidly absorbed and eliminated in the oral (gavage) ADME study. Essentially all of the oral dose was eliminated in 72 hours; 80.2 $\pm$ 8% via urine, 1.6 $\pm$ 0.1% via faeces, and < 0.22% via CO2, and 19.7 $\pm$ 6.1% via the cage wash. At 72 hours after dosing, there was no concentration of the 14C-labelled material in any of the tissues examined including reproductive tissues. Bile duct canulation showed enterohepatic circulation did not occur. Total recovery was 101.8 $\pm$ 3.3%. HPLC analysis of the urine showed that no parent compound was excreted. Approximately 99% of the radioactivity in the urine represented a single metabolite consistent in HPLC retention time with hydroxybenzene sulphonate (phenol sulphonate).

These ADME data indicate that NOBS is very poorly absorbed upon dermal exposure (the anticipated major route of potential exposure) and highly absorbed following oral exposure. Absorbed material appears to be rapidly metabolised (via cleavage of the ester linkage) with excretion of the phenol sulphonate moiety and assumed normal catabolism of the fatty

acid moiety via the established odd-chain fatty acid pattern (AL Lehninger, Biochemistry, 2nd edition, 1975, chapter 20, p.555).

Human Exposure Assessment

Table 8 Consumer Exposure for NOBS used in a Laundry Detergent

Use or Exposure	Estimated Exposure Level	Relevant No Effect Level
Dermal Exposure	4.2×10^{-4} g/kg/day	0.4 g/kg/day
Oral Exposure Drinking Water	3.9×10^{-8} mg/kg/day	1.11 g/kg/day

[3.3] Worker Exposure

There is potential for occupational exposure to this material by workers who either produce the raw material or formulate the laundry detergent containing the material. The potential routes of exposure that are most relevant during manufacture of NOBS and formulation of laundry detergents containing NOBS are dermal and inhalation exposure.

Manufacturing Facility

For workers, exposure to NOBS during the production or transportation process is limited due to process design, industrial hygiene standards and personal protective equipment that are standardly utilitized in production facilities. Employee exposure is minimized through engineering controls, a closed system operation and good industrial hygiene practices to ensure exposure is below an Occupational Exposure Guideline (OEG) of 0.1 mg/m^3. The substance is produced and shipped as a low vapor pressure, non-respirable extrudate preparation with particle size of 500-1000 microns, which further limits the potential for exposure. Dermal exposure is limited by use of personal protective equipment, goggles and impervious gloves worn in direct handling of NOBS and in case of spills, maintenance, cleaning and process intervention.

Formulation Facility

The potential for worker exposure during the manufacture of detergents containing NOBS is minimized through engineering controls, a closed system operation, administrative procedure and personal protective equipment. Periodic monitoring indicates concentrations well below the OEG. All systems which use NOBS are enclosed, maintained under negative pressure, and have sufficient local exhaust ventilation airflow. Good occupational hygiene practices are defined for all operations such as sampling and systems maintenance. Operators involved in these procedures are trained on the potential hazards of the materials, controls and safe practices. Dermal exposure is limited by personal protective equipment, goggles and impervious gloves worn with direct handling of NOBS and in case of spills, maintenance, cleaning and process intervention. A behavior observation and safety sampling system is in place as part of standard operating procedures to reinforce compliance with safe practices. In case of accidental spillage, high efficiency filter portable vacuum cleaners are used routinely for clean up. Processing experience with a variety of

ingredients in the manufacturing of laundry detergents show that the above combination of engineering controls and work practices is effective in minimizing worker exposure.

[3.4] Consumer Residential Exposure

Residential exposure to NOBS from consumer use is expected to be limited based on the use pattern for the product and the chemistry of NOBS. There will be no consistent or significant consumer exposure to unreacted NOBS and the only possible residential exposure to NOBS is through use of laundry products containing this material. Consumer exposure with the tablet form of the product is expected to be the same as or less than with the granular form. In the vast majority of cases, laundry detergent containing NOBS is used in conjunction with an automatic washing machine, which greatly limits potential consumer exposure to unreacted NOBS. The potential routes of consumer exposure are discussed below and are followed by calculations to estimate the most relevant exposures. Consumer monitoring studies have not been performed, as modeled estimates suffice for this material.

[3.4.1] Dermal - The potential sources for dermal exposure when using laundry detergents containing NOBS are 1) during hand laundering, 2) during pretreatment of fabrics with a paste made from detergent, or 3) from skin contact during transfer of the product from the package to the washing machine. The potential for dermal exposure from scooping the product from the package is infrequent and negligible relative to the hand laundering or fabric pretreat scenarios. The transfer of product from the box to the washing machine is completed using a scoop; therefore, the potential for that dermal exposure to NOBS is negligible and of very short duration. Based on insignificant exposure from the latter scenario, exposure calculations are not included. There is no NOBS exposure from residual detergent that may remain on washed fabrics due to the rapid chemical reaction and complete perhydrolysis of this material in the wash water.

Under the typical conditions of the wash, NOBS is converted extremely rapidly to the peroxy compound pernonanoic acid within 3 minutes. Based on the chemistry and timing of this reaction, the following exposure calculations are conservative. In addition, these exposures are of very short duration, in the range of 5-10 minutes per task, which is not considered in the calculations. A summary of the dermal exposure estimates is included in the table below and in more detail in the following section.

Table 9 Consumer Dermal Exposure

Dermal	Exposure	Resulting Dose*
a. Hand Laundry	7.5×10^{-6} g/kg/day	7.5×10^{-8} g/kg/day
b. Fabric Pretreatment	4.1×10^{-4} g/kg/day	4.1×10^{-6} g/kg/day
TOTAL DERMAL EXPOSURE	**4.2×10^{-4} g/kg/day**	**4.2×10^{-6} g/kg/day**

* The resulting dose takes into account the estimated dermal absorption of NOBS which is <1%.

Dermal-Hand Laundering Fabric

Exposure during hand laundry is given by the following equation:

$$\text{Exposure}_{(\text{hand laun.})} = \frac{(\text{tasks/day}) \times (\text{vol. of sol'n on skin}) \times (\text{conc. of HPV substance})}{\text{Body weight}}$$

The dose resulting from this exposure is:

$$\text{Resulting Dose}_{(\text{hand laun.})} = \text{Exposure}_{(\text{hand laun.})} \times \% \text{ absorption}$$

Assumptions:

1. Product is used an average of 0.38 times/day for hand laundry. [1] Therefore,
   (tasks/day) = 0.38
2. The thickness of the wash solution on the skin is 0.0024 cm. [2]
3. The surface area of the hands and forearms is 1900 cm^2. [3]
4. Therefore, the volume of wash solution on the skin =
   (vol. of sol'n on skin) = (0.0024 cm) × (1900 cm^2) = 4.6 cm^3
5. Finished consumer product will contain approximately 6.0% HPV substance.
6. Use concentration of finished consumer product is 0.5%, or 5 mg/ml of wash solution[4]
7. Therefore, concentration of HPV substance in wash solution =
   (conc. of HPV substance) = 5 mg/ml × 0.06% = .30 mg/ml or 3.0×10^{-4} g/cm^3
8. Average adult body weight is 70 kg.

Therefore, exposure during hand laundry is:

$$\text{Exposure}_{(\text{hand laun.})} = \frac{(\text{tasks/day}) \times (\text{vol. of sol'n on skin}) \times (\text{conc. of HPV substance})}{\text{Body weight}}$$

$$= \frac{(0.38 \text{ per day}) \times (4.6 \text{ cm}^3) \times (3.0 \times 10^{-4} \text{ g/cm}^3)}{70 \text{ kg}} = \mathbf{7.5 \times 10^{-6}\ g/kg/day}$$

Percutaneous absorption (% absorption) of substances related to the HPV is less than 1% per ADME study. Therefore the dose resulting from this exposure is:

$$\text{Resulting Dose}_{(\text{hand laun.})} = \text{Exposure}_{(\text{hand laun.})} \times \% \text{ absorption}$$

$$= 7.5 \times 10^{-6} \text{ g/kg/day} \times 1\% = \mathbf{7.5 \times 10^{-8}\ g/kg/day}$$

[1] Unpublished P&G data, multiple studies

[2] Westat, Inc. and Battelle Columbus Laboratories Report to EPA (1985). Subcontract #A-314DS (8149)-270 and contract #68-01-6721. National Household Cleaning and Painting Surveys.

[3] EPA Exposure Factors Handbook, August 1997. Table 6-4, page 6-14.

[4] Unpublished P&G data, HPT #1456-56.

Dermal-Fabric Pretreatment

Exposure during fabric pretreatment is given by the following equation:

$$\text{Exposure}_{(\text{pretreat.})} = \frac{(\text{tasks/day}) \times (\text{vol. of sol'n on skin}) \times (\text{conc. of HPV substance})}{\text{Body weight}}$$

The dose resulting from this exposure is:

$$\text{Resulting Dose}_{(\text{pretreat.})} = \text{Exposure}_{(\text{pretreat.})} \times \% \text{ absorption}$$

Assumptions:

1. Product is used an average of 1 time/day for fabric pretreatment. [5] Therefore, (tasks/day) = 1
2. The thickness of the wash solution on the skin is 0.0024 cm. [6]
3. Fabric pretreatment is done with a skin surface area approximately half the surface area of the palms, or one quarter of the surface area of the hands [7], or $0.08\ m^2 \times 0.25 = 0.02\ m^2$ or $200\ cm^2$.
4. Therefore, the volume of wash solution on the skin = (vol. of sol'n on skin) = $(0.0024\ cm) \times (200\ cm^2) = 0.48\ cm^3$
5. Finished consumer product will contain approximately 6.0% of HPV substance.
6. Finished consumer product is used undiluted for fabric pretreatment (or 1000 mg/ml or $1\ g/cm^3$).
7. Therefore, concentration of HPV substance used for pretreatment = (conc. of HPV substance) = $6.0\% \times 1\ g/cm^3 = 0.06\ g/cm^3$
8. Average adult body weight is 70 kg.

Therefore, exposure during fabric pretreatment is:

$$\text{Exposure}_{(\text{pretreat.})} = \frac{(\text{tasks/day}) \times (\text{vol. of sol'n on skin}) \times (\text{conc. of HPV substance})}{\text{Body weight}}$$

$$= \frac{(1 \text{ per day}) \times (0.48\ cm^3) \times 0.06\ g/cm^3}{70\ kg} = \mathbf{4.1 \times 10^{-4}\ g/kg/day}$$

9. Percutaneous absorption of HPV substance is less than 1% per ADME study. Therefore the dose resulting from this exposure is:

$$\text{Resulting Dose}_{(\text{pretreat.})} = \text{Exposure}_{(\text{pretreat.})} \times \% \text{ absorption}$$

$$= 4.1 \times 10^{-4}\ g/kg/day \times 1\% = \mathbf{4.1 \times 10^{-6}\ g/kg/day}$$

[5] Unpublished P&G data, - MRD 91D520, NHATS.

[6] Westat, Inc. and Battelle Columbus Laboratories Report to EPA (1985). Subcontract #A-314DS (8149)-270 and contract #68-01-6721. National Household Cleaning and Painting Surveys.

[7] EPA Exposure Factors Handbook, August 1997. Table 6-4, page 6-14.

[3.4.2] Oral - There is no anticipated oral exposure under use conditions. Due to the chemistry of NOBS, the potential level in drinking water is negligible to nil. The EFAST model was used to conservatively estimate the concentration of HPV substance in drinking water (assumes perhydrolysis is not complete, that some NOBS remains and none is removed in drinking water treatment facilities). The results of this model indicate the high end (10%ile) drinking water results to be 3.9×10^{-8} mg/kg/day.

The other potential for oral exposure would only occur following accidental ingestion of the product, which would be a one time or infrequent acute exposure. Based on information collected from the Procter & Gamble consumer telephone service, Poison Control Centers and national emergency rooms, when accidental swallowing does occur there are usually no symptoms reported. Occasionally, when symptoms do occur they include nausea, vomiting, or diarrhea, which are mild and transient in nature. These symptoms are not specific to NOBS since they would arise from accidental exposures to product containing NOBS and are symptoms consistent with ingestion of other laundry products.

[3.4.3] Inhalation - Consumer inhalation exposure during use is limited by a number of factors: the low vapor pressure of NOBS, its production in extrudate form, and the overall design of the laundry product as a non-friable, dense granular material. Thus, there is very little dust involved in transferring the product from the package to the washing machine so the potential for inhalation exposure from this action is negligible.

[3.4.4] Aggregate Exposure - As NOBS is a proprietary material, there are no other sources of consumer exposure to this material. As discussed above, there is minimal consumer exposure to NOBS when used in laundry detergents. Even when considering aggregate exposure, the amount of potential total exposure remains low.

[3.4.5] Comparison to E-Fast - To provide a basis for understanding how the results of an assessment conducted by the US EPA for consumer exposure might differ from the P&G assessment, the **E-FAST** model (Exposure and Fate Assessment Screening Tool) was used to evaluate the consumer exposure to NOBS. E-FAST was developed by Versar, Inc. for U.S. EPA's Office of Pollution Prevention, Economics, Exposure and Technology Division. E-FAST provides screening level estimates of concentrations of chemicals released to air, surface water, landfills, and from consumer products and can estimate potential dermal, inhalation and ingestion rates resulting from these releases. Modeled estimates of concentrations and doses are designed to provide high end to bounding estimates of exposure for use in screening level assessments. Information about E-FAST is available via OPPT's Exposure Assessment Tools and Models Web site: www.epa.gov/opptintr/exposure.

E-FAST can be used for a number of consumer product scenarios. NOBS is used in P&G granular laundry detergents, however, E-FAST's Liquid Laundry Detergent scenario was available and used. As discussed in the previous section, the most likely scenarios for consumer exposure to NOBS are skin contact during hand laundering and during use of a concentrated paste for pretreatment of fabric. The exposure estimates from completing the

E-FAST calculations for the use of NOBS at 6% in laundry products are shown in Table 10 and compared to estimates derived from using exposure calculations described earlier and routinely used by Procter & Gamble. A more complete description of this comparison can be found in Appendix C.

Table 10 Comparison of External Exposure Calculated by E-FAST and P&G

Scenario	E-FAST	P&G
Hand Laundry	1.3×10^{-6} g/kg/day	7.5×10^{-6} g/kg/day
Pretreatment	6.6×10^{-4} g/kg/day	4.1×10^{-4} g/kg/day

The above estimates conservatively assume 100% absorption. When there is evidence to support less than 100% dermal penetration the resulting internal dose may be determined by multiplying the external exposure by a dermal penetration fraction. The ADME study found that NOBS was poorly absorbed by the dermal route (less than 1%). E-FAST does not allow for the use of a dermal absorption fraction. Therefore, this needs to be calculated by hand from the E-FAST results, and is shown in Table 11.

Table 11 Comparison of Internal Doses Calculated by E-FAST and P&G

Scenario	E-FAST	P&G
Hand Laundry	1.3×10^{-8} g/kg/day	7.5×10^{-8} g/kg/day
Pretreatment	6.6×10^{-6} g/kg/day	4.1×10^{-6} g/kg/day

Conclusion: The consumer exposure estimates from the E-FAST runs are comparable in magnitude to those estimates derived from typical calculations developed by P&G. Both methods arrived at an external dermal exposure without consideration of dermal penetration of less than 0.01 mg/kg/day from hand laundering of fabrics and less than 1 mg/kg/day for pretreatment for a 6% NOBS granular laundry detergent. The resulting internal dose is less than 0.0001 mg/kg/day from hand laundering and less than 0.01 mg/kg/day for pretreatment. Using either method, the exposure estimates demonstrate very low potential for consumer exposure to NOBS from use of a granular laundry detergent.

[3.5] Human Health Screening Level Assessment

The available data summarized in this document demonstrate that NOBS has a favorable safety profile for use in consumer laundry detergents. The risk to human health is characterized by comparing the estimated exposure to the No Observable Effect Level (NOEL) from animal studies. The amount by which the NOEL exceeds the estimated exposure is referred to as the margin of exposure and this should be sufficiently large to account for several sources of uncertainty and variability in extrapolating data from animal studies to man. Based on the data presented, no adverse effects for humans are expected via any relevant exposure route. The aggregate dermal exposure from hand laundering and

pretreatment of fabrics results in an estimated exposure of 4.2×10^{-4} g/kg/day. In comparing this conservative estimate to the results from the dermal subchronic study where the no effect level (NOEL) is greater than 0.4 g/kg/day, the margin of exposure is acceptable. Even at the highest dose tested in this study (2 ml/kg of a 20% test material solution) there were no systemic effects. The only effect noted was irritation at the site of application, which was dose related and limited the amount that could be repeatedly administered. Studies evaluating the dermal absorption of NOBS showed this material is very poorly absorbed through the skin—less than 1%. For potential oral exposure, if one assumes conservatively that perhydrolysis does not occur, that NOBS would be present in drinking water and not removed in drinking water treatment facilities, the calculated exposure using EFAST would be 3.9×10^{-8} mg/kg/day. The NOEL in an oral dietary study was 1.1 g/kg/day. Comparing the estimated oral exposure to the oral NOEL results in a margin of exposure of many orders of magnitude, even after accommodating inter- and intraspecies variation.

[3.6] References

Biochemistry, 2nd edition. Lehninger, A.L. 1975. 20:555.

Environmental and Human Safety of Major Surfactants. Little, A.D. Arthur D. Little, Inc., Cambridge, Massachusetts. 1991.

Anionic Surfactants. Biochemistry, Toxicology, Dermatology, 2nd edition. Gloxhuber, C. and Kunstler K, eds. Marcel Dekker, Inc. New York. 1992.

Environmental and Human Safety of Major Surfactants. Talmage, S.S. Lewis Publishers, Boca Raton. 1994.

Gerberick, G.F., Robinson, M.K., and Stotts, J. (1993) An Approach to Allergic Contact Sensitization Risk Assessment of New Chemicals and Product Ingredients. Contact Dermatitis, 4(4): 205-211.

Robinson, M.K., Stotts, J., Danneman, P.J., Nusair, T.L. and Bay, P.H.S. (1989) A risk assessment process for allergic contact sensitization. Food Chem. Toxicol. 27:479-489.

AR201-13831B

Robust Summaries

for

Nonanoic acid, sulfophenyl ester, Sodium salt
CAS #: 91125-43-8

Prepared for the HPV Challenge Program by:
The Procter & Gamble Company

December 21, 2001

APPENDIX A: HPV Robust Summaries

1. PHYSICAL-CHEMICAL DATA

[1.1] Melting Point
[1.2] Boiling Point
[1.3] Density (Relative Density)
[1.4] Vapour Pressure
[1.5] Partition Coefficient (n-Octanol/water)
[1.6] Water Solubility
[1.7] Particle Size Distribution

2. ENVIRONMENTAL FATE AND PATHWAYS

[2.1] Photodegradation
[2.2] Stability in Water (Hydrolysis)
[2.3] Biodegradation
[2.4] Ultimate removability
[2.5] Transport between Environmental Compartments

3. ECOTOXICITY

[3.1] Acute Toxicity to Fish
[3.2] Acute Toxicity to Aquatic Invertebrates (Daphnia)
[3.3] Toxicity to Aquatic plants: Algae

4. HUMAN HEALTH TOXICITY STUDIES

SIDS ENDPOINTS

[4.1] Acute Oral Toxicity
[4.2] Acute Percutaneous Toxicity
[4.3] Escherichia coli WP2 and WP2 uvrA Reverse Mutation Assay and Salmonella/ Mammalian - Microsome Mutagenesis Assay (Ames Test)
[4.4] *In vivo* Cytogenetics Study
[4.5] Unscheduled DNA Synthesis (UDS) Test with Mammalian Liver Cells *In vivo*
[4.6] Oral Teratology Study
[4.7] Fertility Study
[4.8] 13 Week Oral (Dietary Administration) Toxicity Study

BEYOND SIDS ENDPOINTS

[4.9] Primary Eye Irritation - Low Volume Eye Test Method
[4.10] Primary Eye Irritation
[4.11] Primary Skin Irritation
[4.12] Delayed Contact Hypersensitivity in Guinea Pigs
[4.13] Dermal Sensitization in Guinea Pigs - Modified Buehler
[4.14] Dermal Sensitization in Guinea Pigs - Modified Buehler
[4.15] Local Lymph Node Assay
[4.16] 28 Day Subchronic Percutaneous Toxicity Study
[4.17] Absorption, distribution, metabolism, and excretion (ADME) study

APPENDIX B: Degradation of NOBS in the wash solution

APPENDIX C: Comparison of P&G to E-FAST Exposure Estimates

APPENDIX D: Exposure Summaries

APPENDIX A: HPV Robust Summaries
PHYSICAL-CHEMICAL DATA

[1.1] Melting Point

Test Substance

Identity:	Nonanoyloxybenzene sulfonate, Na salt (CAS # 91125-43-8; Nonanoic acid, sulfophenyl ester, sodium salt)
Purity:	94.7%
Remarks:	-

Method

Method/guideline followed:	Metal block method according to EEC Directive 67/548, Annex V, A1, as published in 84/449/EEC. The melting point is defined as the temperature at which the phase transition from solid to liquid state, at normal atmospheric pressure, takes place. A small amount of the dried, powdered test substance was packed tightly into a capillary tube. The capillary tube was then placed in the block and the heating rate was adjusted to 4 °C/min until a temperature of 360°C was reached. The physical state of the substance was noted during temperature increase.
GLP:	Yes
Year:	1988
Remarks:	

Results

Melting point:	Did not melt at temperature up to 360°C
Decomposition:	Slowly decomposed over the range 191-350°C
Sublimation:	Not determined
Remarks:	-

Conclusions

Remarks:	As stated in the report: The substance decomposed over the range 191 - 350°C

Data Quality

Reliability (Klimisch Rating):	1
Remarks:	Reliable without restriction, guideline study, GLP

References Report # : P&G 1414/881420

Other

Last changed:	September 5, 2000

Order number for sorting:	
Remarks:	-

[1.2] Boiling Point:

Test Substance

Identity:	-
Purity:	-
Remarks:	-

Method

Method/guideline followed:	-
GLP:	-
Year:	-
Remarks	

Results

Boiling point:	-
Decomposition:	-
Sublimation:	-
Remarks:	-

Conclusions

Remarks:	-

Data Quality

Reliability (Klimisch Rating):	-
Remarks:	-

References -

Other

Last changed:	September 5, 2000
Order number for sorting:	
Remarks:	The boiling point was not assessed as the ingredient slowly decomposed over the range 191-350°C before boiling.

[1.3] Density (Relative Density)

Test Substance

Identity:	Nonanoyloxybenzene sulfonate, Na salt (CAS # 91125-43-8; Nonanoic acid, sulfophenyl ester, sodium salt)
Purity:	94.7%
Remarks:	-

Method

Method/guideline followed:	Pycnometer method as described in ISO Recommendation R1183 used in accordance with EEC Directive 67/548, Annex V, A3, as published in 84/449/EEC. The relative density (D^{20}_{4}) is defined as the ratio of the mass of a volume of substance to be examined, determined at 20°C, and the mass of the same volume of water at 4°C.
GLP:	Yes
Year:	1988
Remarks:	

Results $D^{20}_{4} = 1.236$

Conclusions

Remarks:	As stated in the report: The relative density of the substance was determined as 1.236

Data Quality

Reliability (Klimisch Rating):	1
Remarks:	Reliable without restriction, guideline study, GLP

References Report # : P&G 1414/881420

Other

Last changed:	September 5, 2000
Order number for sorting:	
Remarks:	-

[1.4] Vapour Pressure

Test Substance

Identity:	Nonanoyloxybenzene sulfonate, Na salt (CAS # 91125-43-8; Nonanoic acid, sulfophenyl ester, sodium salt)
Purity:	94.7%
Remarks:	-

Method

Method/guideline followed:	Vapour pressure according to EEC Directive 67/548, Annex V, A4, as published in 84/449/EEC. The vapour pressure is defined as the saturation pressure above a solid or liquid substance. At the thermodynamic equilibrium, the vapour pressure of a pure substance is a function of temperature only.
GLP:	Yes
Year:	1988
Remarks:	-

Results

Vapor Pressure value:	1.71×10^{-7} Pa
Temperature °C:	25°C
Decomposition:	No

Conclusions

Remarks:	As stated in the report: The result was considered reliable in absolute terms to two orders of magnitude.

Data Quality

Reliability (Klimisch Rating):	1
Remarks:	Reliable without restriction, guideline study, GLP

References Report # : P&G 1414/881420

Other

Last changed:	September 5, 2000
Order number for sorting:	-
Remarks:	-

[1.5] Partition Coefficient (n-Octanol/water)

Test Substance

Identity:	Nonanoyloxybenzene sulfonate, Na salt (CAS # 91125-43-8; Nonanoic acid, sulfophenyl ester, sodium salt)
Purity:	94.7%
Remarks:	-

Method

Method/guideline followed:	The partition coefficient (n-octanol/water) was determined according to EEC Directive 67/548, Annex V, A8, as published in 84/449/EEC. The partition coefficient pressure is defined as the ratio of its equilibrium concentrations in a two phase system consisting of two largely immiscible solvents, in this study n-octanol and water.
GLP:	Yes
Year:	1988
Remarks:	-

Results

Log Pow:	- 0.572
Temperature °C:	24.5°C
Remarks:	The substance is not surface active, dissociative, or insoluble in water

Conclusions

Remarks:	As stated in the report: The partition coefficient (n-octanol/water) was determined as Log Pow = - 0.572 at 24.5°C

Data Quality

Reliability (Klimisch Rating):	1
Remarks:	Reliable without restriction, guideline study, GLP

References Report # : P&G 1414/881420

Other

Last changed:	September 5, 2000
Order number for sorting:	-
Remarks:	-

[1.6.] Water Solubility

Test Substance

Identity:	Nonanoyloxybenzene sulfonate, Na salt (CAS # 91125-43-8; Nonanoic acid, sulfophenyl ester, sodium salt)
Purity:	94.7%
Remarks:	-

Method

Method/guideline followed:	Flask stirring method as described in EEC Directive 67/548, Annex V, A6, as published in 84/449/EEC. Solubility in water is specified by the saturation mass concentration of the substance in water at a given temperature. The solubility in water is specified in units of mass per volume of solution.
GLP:	Yes
Year:	1988
Remarks:	-

Results

Solubility in water:	245 ± 8 g/L at 20 ± 0.5 °C
Description of solubility:	Soluble
pH value, concentration, temperature:	7.02 (pH), 253 g/L at 30°C
pKa value at 25 °C	Not applicable

Conclusions

Remarks:	Solubility in water was determined as 245 ± 8 g/L (average and standard deviation of the results of three tests) at 20 ± 0.5 °C

Data Quality

Reliability (Klimisch Rating):	1
Remarks:	Reliable without restriction, guideline study, GLP

References Report # : P&G 1414/881420

Other

Last changed:	September 5, 2000
Order number for sorting:	-
Remarks:	-

[1.7] Particle size distribution:

Test Substance

Identity:	Nonanoyloxybenzene sulfonate, Na salt (CAS # 91125-43-8; Nonanoic acid, sulfophenyl ester, sodium salt)
Purity:	77.5%
Remarks:	white pellets

Method

Method/guideline followed:	CIPAC, Analysis of Technical and Formulated Pesticides, MT 170: "Dry Sieve Analysis of Water Dispersible Granules", CIPAC Handbook Volume F, 1995
GLP:	Yes
Year:	1999
Remarks	The interval of the mesh size in which at least 80% of the test substance is collected was determined. Analytical balance sensitive to 0.01g. (type PE 3600; Mettler-Toledo B.V., Tiel, The Netherlands)

Results

Particle size distribution:

Sieve (microm.)	% substance collected
Receiver pan	0.17
500	49.49
850	48.50
1000	1.79
2000	0.05

Remarks: -

Conclusions

Remarks: The interval of the mesh size in which at least 80% (>97%) of the test substance was collected, was 500 – 1000 μm.

Data Quality

Reliability (Klimisch Rating):	1
Remarks:	Reliable without restriction, guideline study, GLP

References	NOTOX B.V., ‘s-Hertogenbosch, The Netherlands. Report # : NOTOX Project 270844, NOTOX Susbstance 94113

Other

Last changed:	September 3, 2001
Remarks:	-

2. ENVIRONMENTAL FATE AND PATHWAYS

[2.1] Photodegradation

Test Substance

Identity:	-
Purity:	-
Remarks:	-

Method

Method/guideline followed:	-
GLP:	-
Year:	-
Remarks	

Results

Melting point:	-
Decomposition:	-
Sublimation:	-
Remarks:	-

Conclusions

Remarks:	-

Data Quality

Reliability (Klimisch Rating):	-
Remarks:	-

References -

Other

Last changed:	September 5, 2000
Order number for sorting:	-
Remarks:	Photodegradation was not assessed. Study not relevant— material has low volatility, is degraded in the wash; residual is rapidly and completely biodegraded and highly removed during wastewater treatment

[2.2] Stability in Water (Hydrolysis)

Test Substance

Identity:	Nonanoyloxybenzene sulfonate, Na salt (CAS # 91125-43-8; Nonanoic acid, sulfophenyl ester, sodium salt)
Purity:	77.5%
Remarks:	-

Method

Method/guideline followed:	Solutions of 10mg/L, 100mg/L and 8g /L were prepared in deionised water (pH were respectively 6.4, 5.3 & 4.2) and were kept at 20°C on a bench. Aliquots were collected at various time intervals up to 192 hours and stored at -15°C till analysis. Residual concentration was determined by FI/MS/MS (Flow Injection/Mass Spectrometry/ Mass Spectrometry) for the solutions of 10 & 100mg /L and estimated by direct single $CatSO_3$ (total anionic content by a two-phase titration) for the 8g /L solution.
GLP:	No
Year:	1999
Remarks:	Duration: 192 hours Positive Controls: The calibration standards were dissolved in water/acetonitrile 50/50 v/v to obtain solutions in the µg/L range. Negative Controls: water/acetonitrile 50/50 v/v Analytical procedures: FI/MS/MS and direct single $CatSO_3$ (total anionic content by a two-phase titration) Presence of an undissolved material.

Results

Nominal value:	10 mg/L
Measured value:	7.3 mg/L after 192 hours
Degradation %:	27 % at pH 6.4 at 20°C after 192 hours
Nominal value:	100 mg/L
Measured value:	89 mg/L after 192 hours
Degradation %:	11 % at pH 5.3 at 20°C after 192 hours
Nominal value:	8 g/L
Measured value:	7.7 g/L after 168 hours
Degradation %:	4 % at pH 4.2 at 20°C after 168 hours
Breakdown products:	no
Remarks:	The undissolved material was further extracted in hexane and analysed by FI/MS for qualitative analysis. The main identified compounds were nonanoic and hexadecanoïc acid. Minor other

	fatty acids (C10, 12, 14 & 18) were also detected. Cloudiness observed in toxicity tests was probably due to the presence of these fatty acids as impurities in the raw material rather that precipitation of the test substance.
Conclusions	
Remarks:	Submitter comment: The substance is stable in water at pH<7 for a few days
Data Quality	
Reliability (Klimisch Rating):	1, Reliable without restriction, comparable to guideline study
Remarks:	-
References	S. Peeters, lab notebook ETS 775 pages 81 to 88 & 91-92, The Procter & Gamble Company, European Technical Center, Belgium
Other	
Last changed:	September 7, 2000
Order number for sorting:	-
Remarks:	-

[2.3] Biodegradation

Test Substance

Identity:	Nonanoyloxybenzene sulfonate, Na salt (CAS # 91125-43-8; Nonanoic acid, sulfophenyl ester, sodium salt)
Purity:	98.3%
Remarks:	-

Method

Method/guideline followed:	OECD 301B. CO_2 production measured as the percentage of theoretical CO_2 ($ThCO_2$), calculated from the organic carbon content of the test substance
Test type:	Aerobic conditions
GLP:	Yes
Year:	2000
Contact time:	28 days
Inoculum:	The inoculum (10^8 cells/L) was not pre-adapted to the test substance.
Remarks:	The inoculum was activated sludge from an aeration tank of the waste water treatment plant of Zonhoven (Belgium). The test substance concentration was 10 mg C L^{-1} tested in duplicate. Temperature varied between 18 and 22°C. Direct addition of the test substance. Samples were collected before, then 2, 3, 4, 6, 8, 10, 15, and 28 days after addition of the test substance. Sodium benzoate was used as a positive control. Sodium benzoate + the test substance was used as a toxicity control. Deionized water with low carbon content was used for blank measurements. The two biodegradation values of the replicates were not averaged.

Results:

Degradation, test substance:	Theoretical CO_2: 84 and 89% (replicates 1 and 2, respectively) after 28 days. DOC removal: 96% and 96% (replicates 1 and 2, respectively) after 28 days.
Degradation, positive control:	Theoretical CO_2: 87% after 28 days. DOC removal: 96% after 28 days.
Degradation, toxicity control:	Theoretical CO_2: 83% and 84% (replicates 1 and 2, respectively) after 28 days. DOC removal: 97% and 97% (replicates 1 and 2, respectively) after 28 days.
Breakdown products:	No
Remarks:	No lag time, no inhibition, no excessive standard deviation, half-life: 4 to 5 days, time required for

	10% degradation: 3 days, total degradation at the end of the test: see above. Test substance would be classified as Readily Biodegradable in the EU.
Conclusions	
Remarks:	86% CO2 was produced within 28 days. 10% CO_2 production was achieved by day 3. By day 13, CO_2 production was over 70%. Test substance would be classified as Readily Biodegradable in the EU.
Data Quality	
Reliability (Klimisch Rating):	1, Reliable without restriction, guideline study, GLP
Remarks:	-
References	LISEC Report # : WB-04-124, Craenevenne 140, 3600 Genk, Belgium, Study Director: Dr M. Indeherberg
Other	
Last changed:	September 13, 2000
Order number for sorting:	-
Remarks:	-

[2.4] Ultimate removability

Test Substance

Identity:	Nonanoyloxybenzene sulfonate, Na salt (CAS # 91125-43-8; Nonanoic acid, sulfophenyl ester, sodium salt)
Purity:	94.7%
Remarks:	-

Method

Method/guideline followed:	OECD 302A. Objective of the test is to determine the removability of the test material in the Semi-Continuous Activated Sludge (SCAS) test system, as measured by soluble organic carbon. The % carbon remaining = 100 x ((C concentration in test unit-average C concentration in blank)/(Test material C concentration added to test unit)).
Test type:	SCAS
GLP:	Yes
Year:	1984
Inoculum:	Avondale Sewage Treatment plant, Avondale PA
Test period:	7 days
Test concentration:	20 mg C/l
TOC stock solution:	0.534 mg C/mg active (0.533 at end of test)
Test temperature:	22-24°C
Remarks:	

Results:

Average % removal, DOC:	99.7%
95% confidence interval:	2.0%
Remarks:	

Conclusions

Remarks:	Author comment: The endpoint has been adequately characterized.

Data Quality

Reliability (Klimisch Rating):	1, Reliable without restriction, guideline study, GLP
Remarks:	-

References WESTON Report # : 84-007, West Chester, PA, USA, Study Director: Dr JD Curry

Other

Last changed:	October 17, 2000
Order number for sorting:	-
Remarks:	Ultimate removability is not a typical SIDS endpoint but was included in the list of robust summaries since this test provides additional information to predict NOBS environmental concentration.

[2.5] Transport between Environmental Compartments (Fugacity)

Test Substance

Identity:	Nonanoyloxybenzene sulfonate, Na salt (CAS # 91125-43-8; Nonanoic acid, sulfophenyl ester, sodium salt)

Method

Method/guideline followed:	
Test type:	Level III Fugacity Model, v1.01, MacKay, 1996. Emissions (1000 kg/hr) to water using standard defaults and physical/chemical properties documented in this report.
Year	2000

Results:

Distribution:	Air	2.5×10^{-18} %
	Water:	99.9%
	Sediment:	0.13%
	Soil:	3×10^{-10} %
Remarks:	This is the currently accepted model for theoretical estimation.	

Conclusions

Remarks:	This material is predicted to be distributed to surface waters.

Data Quality

Reliability (Klimisch Rating):	2. Accepted method of estimation
Remarks:	

References

Other

Last changed:	October 17, 2000
Order number for sorting:	-
Remarks:	

3. ECOTOXICITY

[3.1] Acute Toxicity to Fish

Test Substance

Identity:	Nonanoyloxybenzene sulfonate, Na salt (CAS # 91125-43-8; Nonanoic acid, sulfophenyl ester, sodium salt)
Purity:	96.8%
Remarks:	-

Method

Method/guideline followed:	Acute toxicity to fish, EPA-660/3-75-009
Test type:	96h Static
GLP:	No
Year (study performed):	1982
Species/Strain/Supplier:	*Lepomis macrochirus* (bluegill), Bionomics lot # 82A12. Commercial fish supplier in Connecticut
Analytical monitoring:	Nominal
Exposure period:	96h
Statistical methods:	LC50 values estimated using moving average angle analysis (Stephan 1978).
Remarks:	Test fish (Age/length/weight, loading, pretreatment): Age not provided, 30 mm, 0.27 g, 10 fish per test jar, held in a 500 L fiberglass tank under a photoperiod of 16 hours light and 8 hours darkness. Fed a dry pelleted food, ad libitum, daily, except during the 48 hours prior to testing. Details of test: Static Dilution water source: Soft water reconstituted from deionized water according to US EPA (1975) Dilution water chemistry: hardness: 42 mg $CaCO_3$/L, alkalinity: 30 mg $CaCO_3$/L, pH: 7.7, TOC, TSS, and salinity not reported (freshwater) Stock and test solution: Clear colorless working stock solution of 15 mg active ingredient/mL was prepared. Appropriate volume of stock solution was then added to each test jar and mixed by stirring with a glass rod. Vehicle/solvent: Not used. Stability of the test chemical solutions: Test substance stable in water for > 96 h (see 3.1.2. above). Exposure vessel type: photoperiod of 16 hours light and 8 hours darkness, no aeration, 15 L Number of replicates, fish per replicate: 1 test jar per concentration, 10 fish per jar.

Water chemistry in the control: D.O: 4.5 to 8.6 mg/L; pH: 7.0 to 7.7
Water chemistry where effects were observed: D.O: 1.2 to 8.3 mg/L; pH: 6.8 to 7.7. D.O. dropped below 20% saturation after 48 h. It is at that time that mortality occurred.
Test temperature: 22 °C

Results:

Nominal concentrations: control; 17; 28; 46; 78; 130 $mg.L^{-1}$
Measured concentrations: Not measured
Unit: $mg.L^{-1}$
Element value: LC50, 96 hours, based on nominal concentrations
Statistical results: described below
Remarks: Biological observations: All exposed fish were respiring rapidly
Table showing cumulative mortality; data between brackets are D.O. levels expressed as % saturation:

Conc. (mg/L)	0h (%)	24h (%)	48h (%)	72h (%)	96h (%)
130	0 (97)	0 (76)	60 (32)	100 (23)	100 (-)
78	0 (99)	0 (74)	70 (27)	90 (22)	90 (23)
46	0 (97)	10 (69)	40 (16)	40 (10)	50 (15)
28	0 (94)	0 (64)	30 (17)	50 (14)	60 (16)
17	0 (100)	0 (76)	0 (40)	10 (26)	20 (33)
Control	0 (98)	0 (75)	0 (60)	10 (51)	10 (58)

Lowest concentration 100% mortality: 130 mg/L
Mortality of controls: up to 10%
Abnormal responses: -
Reference substance: Na lauryl sulfate, 96h-LC50 = 4.9 mg/L
Observations: All test solutions were cloudy after 48hrs. During a subsequent study on stability in water (see 3.1.2. above), the undissolved material was further extracted in hexane and analysed by FI/MS for qualitative analysis. The main identified compounds were nonanoïc and hexadecanoïc acid. Minor other fatty acids (C10, 12, 14 & 18) were also detected. The fatty acids level in the tested raw material was < 2.4%. Cloudiness observed in toxicity tests was probably due to the presence of these fatty acids as impurities in the raw material rather that precipitation of the test substance.
Endpoint value: LC50 = 32 $mg.L^{-1}$

Conclusions

Remarks: The reported fish mortality was mainly the result of stress due to low oxygen level. Author

	comment: The endpoint has been conservatively characterized.
Data Quality	
Reliability (Klimisch Rating):	2, Comparable to guideline study with acceptable restrictions. Not GLP
Remarks:	-
References	EG&G Bionomics, 790 Main street, Wareham, Massachusetts, Report # : BW-82-7-1222; Stephan C (1978) US EPA, Environmental Research Laboratory, Duluth, Minnesota, Personal communication. US EPA (1975) Ecological research series (EPA-660/3-75-009), 61 p.
Other	
Last changed:	September 13, 2000
Order number for sorting:	-
Remarks:	-

[3.2] Acute Toxicity to Aquatic Invertebrates (Daphnia)

Test Substance

Identity:	Nonanoyloxybenzene sulfonate, Na salt (CAS # 91125-43-8; Nonanoic acid, sulfophenyl ester, sodium salt)
Purity:	96.8%
Remarks:	-

Method

Method/guideline followed:	Acute toxicity to invertebrates, EPA-660/3-75-009
Test type:	48h Static
GLP:	No
Year (study performed):	1982
Analytical procedures:	Nominal concentrations
Species/Strain:	*Daphnia magna*
Test details:	Static, Single initial dosing
Statistical methods:	LC50 values estimated using moving average angle analysis (Stephan 1978).
Remarks:	Test organisms: were obtained from laboratory stocks cultured at EG&G, Bionomics. Age of the test organisms at study initiation was ⌠ 24h. Test conditions: For each test concentration, the appropriate amount of the test substance was added directly to 1L dilution water and the solution was vigorously mixed on a magnetic stirrer for 30 seconds. The set of control beakers contained the same dilution water and was maintained under the same conditions as the beakers for exposure, but were not dosed with the test substance. Test solutions were not aerated. Based on a subsequent study on stability in water (see 3.1.2. above), the test substance is expected to have been stable during the test. Test temperature range was 22 ± 1°C. Exposure vessel type: The toxicity test was conducted in 250 mL beakers each of which contained 200 mL of test solution. The dilution water used was fortified well water and had the same quality as the culture water. Dilution water source: The culture water was prepared by fortifying well water according to the formula for hard water presented by US EPA (1975) and filtering it through an Amberlite XAD-7 resin column to remove any potential organic contaminants.

Dilution water chemistry: This water had a total hardness and alkalinity as calcium carbonate ($CaCO_3$) of 160 ± 20 mg/L and 110 ± 10 mg/L, respectively; a pH range of 7.9-8.3; a dissolved oxygen concentration > 5.3 mg/L (i.e., 60% saturation).
Lighting: The test area was illuminated with Durotest (Optima) fluorescent lights at an intensity of 100-150 footcandles (as stated in the report).
Water chemistry in the control: D.O. 8.3 mg/L, pH 8.4; at test substance concentration of 1 g/L: D.O. 7.8-8.6 mg/L, pH 7.5-8.2.
Element basis (i.e., immobilization): EC50 (mg/L)
Test design: 3 replicates were used for each test concentration. 15 daphnia were randomly distributed to each concentration (5 fleas per replicate). Nominal concentrations: control; 50; 80; 120; 220; 360; 600; 1000 $mg.L^{-1}$. Exposure period: 48h.

Results:

Nominal concentrations:	control; 50; 80; 120; 220; 360; 600; 1000 $mg.L^{-1}$
Measured concentrations:	Not measured
Unit:	$mg.L^{-1}$
EC50, at 24 and 48 hours:	> 1000 $mg.L^{-1}$, > 1000 $mg.L^{-1}$
Statistical results:	The EC50 was empirically estimated to be > 1000 $mg.L^{-1}$, the highest concentration tested.
Remarks:	Biological observations: Several daphnia had undissolved test material attached to their carapace. During a subsequent study on stability in water (see 3.1.2. above), the undissolved material was further extracted in hexane and analyzed by FI/MS for qualitative analysis. The main identified compounds were nonanoïc and hexadecanoïc acid. Minor other fatty acids (C10, 12, 14 & 18) were also detected. Cloudiness observed in toxicity tests was probably due to the presence of these fatty acids as impurities in the raw material rather that precipitation of the test substance.

Immobilized/exposed daphnids: 8/105
Concentration response: EC50 > 1000 $mg.L^{-1}$, confidence interval not stated.
Cumulative immobilization: 40% were immobilized at 1000 $mg.L^{-1}$, 7% were immobilized at 600 $mg.L^{-1}$, none were immobilized at lower concentrations.

	Control response satisfactory: Yes
Conclusions	
Remarks:	Author comment: The endpoint has been adequately characterized.
Data Quality	
Reliability (Klimisch Rating):	2, Reliable with restriction due to the static renewal protocol. Actual exposure concentrations might have been < nominal values, though during a subsequent study on stability in water (see 2.2. above), the test substance was shown to be stable in water. Not GLP
Remarks:	-
References	EG&G Bionomics, 790 Main street, Wareham, Massachusetts, Report # : BW-82-7-1221; US EPA (1975) Ecological research series (EPA-660/3-75-009), 61 p.
Other	
Last changed:	September 13, 2000
Order number for sorting:	-
Remarks:	-

[3.3] Toxicity to Aquatic plants: Algae

Test Substance

Identity:	Nonanoyloxybenzene sulfonate, Na salt (CAS # 91125-43-8; Nonanoic acid, sulfophenyl ester, sodium salt)
Purity:	98.3%
Remarks:	-

Method

Method/guideline followed:	Toxicity to algae; OECD Guideline 201
Test type:	72h static
GLP:	Yes
Year (study performed):	1999
Species/strain # and source:	*Selenastrum capricornutum*, LISEC laboratory culture (ex. CCAP 278/4)
Element basis:	The concentration of the test substance that resulted in a 50% reduction in either growth (EbC50) or growth rate (ErC50) relative to the control.
Exposure period:	72h
Analytical monitoring:	Analytical confirmation of exposures with Flow Injection - Mass Spectrometry (FI/MS/MS). Sampling times: at the start and after 24, 48, 72h. 3 mL samples for all test concentrations. Formaldehyde (1%) added and acidification with HCl (pH 4).
Test details:	Static, Single initial dosing
Statistical methods:	EC50 and NOEC values were calculated incorporating measured exposure concentrations (geometric means, Probit method). For ECx value calculations, the statistical model was fitted to data using the SAS procedure NLIN. For NOEC value calculations, the statistical model was fitted to data using the SAS procedure GLM.
Remarks:	Microscopic observation revealed no deformed or abnormal algae cells in the pre-culture. The algal medium (recommended in OECD Guideline 201) was buffered to pH 7 by blowing 0.5% CO_2 in air into the medium solution. The test included 3 controls containing only algae and medium, 3 replicates at each concentration, containing algae, medium and test substance, and 1 reference test vessel for each test concentration containing the algal medium and the test substance. Temperature was recorded daily during the test in 1 replicate of each test concentration. Growth/test medium included $NaHCO_3$: 50 mg/L, pH7.1,

$Na_2EDTA.2H_2O$. Deionized water was used as dilution water source. Test containers were 250 mL glass flasks covered with a plastic stop. 100 mL of test solution were used in each flask. Solutions were shaken once a day before the spectrophotometrical measurement.
pH in test

Nominal conc.	pH at time (h)	
	0	72
Control	7.1	7.1
2 mg/L	7.1	7.1
4.5 mg/L	7.1	7.0
10 mg/L	7.1	7.0
23 mg/L	7.1	7.0
50 mg/L	7.0	6.9

Mean measured concentrations are expressed as geometric means.

Results:

Nominal concentrations:	control, 2, 4.5, 10, 23, 50 mg/L
Mean measured concentrations:	0.05, 0.19, 0.38, 0.91, 4.6, 35.5 mg/L
Unit:	$mg.L^{-1}$
Element value:	ErC50 = 26.3 $mg.L^{-1}$ at 72 hours; EbC50 = 9.3 $mg.L^{-1}$ at 72 hours.
NOEC:	biomass: 0.38 mg/L, rate: 0.91 mg/L
Control response satisfactory?	Yes
Statistical results:	ErC50 95% confidence interval: 18.2 - 38.0 at 72 hours; EbC50 95% confidence interval: 7.2 - 11.8 at 72 hours.
Remarks:	Inhibition: at 2 mg/L: biomass: 0.9%, growth rate: -3.8%, at 4.5 mg/L: biomass: 6.9%, growth rate: -2.4%, at 10 mg/L: biomass: 14%, growth rate: 3.7%, at 23 mg/L: biomass: 39%, growth rate: 29%, at 50 mg/L: biomass: 70%, growth rate: -50%.

Conclusions

Remarks:	The concentrations of the test substance that caused 50% reduction in biomass (EbC50, 0-72h) and inhibition of growth rate (ErC50, 0-72h) of *S. capricornutum* with respect to a control culture were 9.3 mg/L (95% confidence interval: 7.2 - 11.8), and 26.3 mg/L (95% confidence interval: 18.2 - 38.0), respectively. The No-Observed-Effect-Concentration for biomass and growth rate after 72h were 0.38 mg/L and 0.91 mg/L, respectively. Author comment: The endpoints have been adequately characterized.

Data Quality

Reliability (Klimisch Rating):	1, Reliable without restriction, guideline study, GLP
Remarks:	-
References	LISEC Report # : WE-06-248, Craenevenne 140, 3600 Genk, Belgium, Study Director: Dr M. Indeherberg; Analytico Report # : 4499060006, Berschot 69-71, 4817 PR Breda, P.O. Box 9910, The Netherlands.

Other

Last changed:	September 15 2000
Order number for sorting:	-

[4] HUMAN HEALTH TOXICITY STUDIES

SIDS ENDPOINTS

[4.1] Acute Oral Toxicity

Study Title	Acute Oral Toxicity(LD_{50}) Study
Date	October 22, 1982
Test Facility	Miami Valley Laboratories, Procter & Gamble Cincinnati, OH USA
GLP Compliance	Yes; EPA
Test Material	Sodium Nonanoyloxybenzene Sulfonate (NOBS, administered as a 40% w/v aqueous suspension)
Animal Species	Rat, Sprague-Dawley CD Prefasted body weights 190-300 grams
Number of Animals	10 rats /group (5 males, 5 females); 4 groups
Dosing	Oral gavage; 40% w/v (in distilled water) suspension used for each dose level, 5.10, 5.78, 6.46, and 7.14 g test material/kg body weight. Animals were fasted for 18-20 hours prior to dosing.
Observations	All animals were observed for mortality and clinical signs of toxicity at 0.5, 1, 2, 3 and 4 hours after dosing and daily thereafter for 14 days.
Results and Discussion	The oral LD_{50} for male and female rats (combined Probit method) was calculated to be 6.03 g/kg body weight (95% confidence limits: 5.62 - 6.44 g/kg). All mortality occurred within two days following administration of the test material (see table below). Clinical signs observed included diarrhea, abdominal gripping, hypoactivity and decreased respiratory rate. Generally, the signs and number of animals involved appeared to be dose related. All rats that died during the study had irritation or hemorrhaging of the stomach and intestines, consistent with irritation observed with other related surfactants .
Conclusion	The acute oral LD_{50} in rats is 6.03 g/kg.
Klimisch criterium	1

Mortality Summary (Number of Deaths)

Dosage Level	Days Post Administration															
	1		2		3		4		5		6		7-14		Total	
g/kg	M	F	M	F	M	F	M	F	M	F	M	F	M	F	M	F
5.10	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
5.78	1	5	0	0	0	0	0	0	0	0	0	0	0	0	1	5
6.46	2	4	0	0	0	0	0	0	0	0	0	0	0	0	2	4
7.14	1	2	3	3	0	0	0	0	0	0	0	0	0	0	4	5

[4.2] Acute Percutaneous Toxicity

Study Title	Acute Percutaneous Toxicity (Rabbits) APCT
Date	September 21, 1982
Test Facility	Miami Valley Laboratories, Procter & Gamble Cincinnati, OH USA
GLP Compliance	Yes
Test Material	Sodium Nonanoyloxybenzene Sulfonate (NOBS, administered as a 40% w/v aqueous suspension)
Animal Species	New Zealand White Rabbits; body weights 2.0 - 3.5 kg
Number of Animals	6 rabbits/group (3 males, 3 females) in 2 groups of 3 animals each
Dosing Route/ Regimen	A 40% w/v aqueous solution of the test material (2 ml/kg body weight) was applied dermally to the back. Prior to treatment, hair was clipped from shoulder to rump exposing an area approximately 15 cm wide. The skin of 3 animals was left intact and the skin of the other 3 animals was abraded (exposure of the horny layer of epidermis without causing bleeding). Test material was spread evenly over the prepared skin and immediately covered with 8-ply gauze held in place by a impermeable dressing covering the entire trunk. At the end of the 24 hour exposure period, dressings were removed and the treated area of the skin gently wiped to remove residual material.
Observations	All animals were observed for mortality and clinical signs at 24 hours after dosing and daily thereafter for 14 days. Dermal effects were assessed daily according to a defined grading scale for erythema, edema and eschar. All animals were necropsied either upon death or at the end of the 14 day observation period for gross morphologic alterations. Tissues representing gross lesions (other than treatment area skin) were collected for histological examination if the alteration was of possible treatment origin.

Results and Discussion	One animal from the abraded group died on Day 7 of non-treatment related causes (gastro-enteritis of unknown etiology). During the first 6 days following test material administration, dermal irritation range from moderate (1 of 6 sites) to severe (5 of 6 sites) erythema, moderate edema (6 of 6 sites) and slight atonia. Only slight erythema was observed beyond Day 7. All animals gained weight. Except for the local skin effects observed at the site of application, no treatment related gross or histopathological effects were observed at necropsy.
Conclusions	The dermal LD_{50} in rabbits is greater than 2.0 ml/kg (0.8 g/kg)
Klimisch criterium	1

[4.3] Escherichia coli WP2 and WP2 uvrA Reverse Mutation Assay and Salmonella/ Mammalian - Microsome Mutagenesis Assay (Ames Test)

Study Title	Escherichia coli WP2 and WP2 uvrA Reverse Mutation Assay and Salmonella/ Mammalian - Microsome Mutagenesis Assay (Ames Test)
Date	October 13, 1983
Test Facility	Microbiological Associates Bethesda, MD, USA
GLP Compliance	Yes; EPA
Test Material	Sodium Nonanoyloxybenzene Sulfonate
Animal Species	E. coli and Salmonella (TA1535, TA100, TA1537, TA1538 TA98)
Number of Animals	Not applicable
Dosing	Test material concentrations ranged from 50 to 20,000 µl per plate in the preliminary toxicity dose range finding studies and typically 50 to 7,000 µl per plate in the definitive studies. Appropriate positive, solvent and sterility controls were used. Tester strain titers were determined. All dose levels of test material, solvent and positive controls were plated in triplicate.
Observations	Following an approximate 48 hour incubation at 37 C, revertant colonies per plate were counted; for all replicate plating, mean revertant colonies per plate were calculated.
Results and Discussion	The results of the E. coli and Salmonella/mammalian microsome reverse mutation assays (Plate Incorporation Method) indicate that under the conditions of these studies, the test material did not cause a positive response on any of the tester strains in the presence or absence of Arochlor-induced rat liver microsomes.
Conclusion	The test material is not mutagenic.
Klimisch criterium	1

[4.4] *In vivo* Cytogenetics Study

Study Title	*In vivo* Cytogenetics Study in Rats: Compound E1235.01
Date	February 23, 1983
Test Facility	EG&G/ Mason Research Institute Worcester, MA USA
GLP Compliance	Yes; EPA
Test Material	Sodium Octanoyloxybenzene Sulfonate (C8 AOBS) -50% Sodium Decanoyloxybenzene Sulfonate (C10 AOBS) -50%
Animal Species	Charles River Sprague Dawley Rats
Number of Animals	120 total 3 animals/sex/dose group/sacrifice time point 5 dose groups (negative control, positive control, high dose, mid dose, and low dose)
Dosing Route/ Regimen	Negative control - distilled water Positive control - methylmethane sulfonate Acute dosing regimen - doses 3.2, 1.1, or 0.32 g/kg C8/10 AOBS sacrifice times 6, 24, or 48 hours post dose Chronic dosing regimen - doses 1.6, 0.5, or 0.16 g/kg C8/10 AOBS for 5 days An i.p. injection of colchicine was given to inhibit mitosis ~ 2 hours prior to sacrifice. Bone marrow was collected, fixed, stained, and analyzed.
Observations	Many animals dosed acutely with mid and high dose levels showed some signs of toxicity such as diarrhea or exudate. In the subchronic group, few animals showed symptoms such as dyspnea and inactivity (including positive control group).
Results and Discussion	The appropriate positive and negative controls indicate a valid test. The results of this study indicate that C8/10 AOBS, administered orally over the dose range of 0.32 - 3.2 g/kg for the acute study and 0.16 - 1.6 g/kg for the subchronic study, did not induce a statistical increase in the number of chromosomal aberrations.
Conclusion	The test compound has no clastogenic potential under the conditions of this test.
Klimisch criterium	1

[4.5] Unscheduled DNA Synthesis (UDS) Test with Mammalian Liver Cells *In vivo*

Study Title	Unscheduled DNA Synthesis (UDS) Test with Mammalian Liver Cells *In vivo*
Date	October 3, 2000
Test Facility	BioReliance Rockville, MD
GLP Compliance	Yes
Test Material	Nonanoyloxybenzene sulfonate (NOBS extrudate: 78% C9 AOBS)
Animal Species	Sprague Dawley rats
Number of Animals	50 male rats total 10 animals dose group 5 dose groups (negative control, positive control, high dose, mid dose, and low dose)
Dosing Route/ Regimen	Negative control - sterile distilled water Positive control - Dimethylnitrosamine (DMN), 35 mg/kg bw NOBS 2,000 mg/kg bw NOBS 1,000 mg/kg bw NOBS 500 mg/kg bw The test article-vehicle mixture, negative control and positive control were administered via gavage at a constant volume of 10 mL/kg bw. All rats in the experimental and control groups were weighed immediately prior to dose administration and the dose volume was based on individual body weights.
Observations/ Procedures	Animals were observed after dose administration for clinical signs of toxicity. Hepatocytes were harvested at either 2-4 post dose or 12-16 hours post dose. In preparation of hepatocyte cultures, rats were anesthetized and livers were perfused. A minimum of 6 cultures were set up for reach rat. Ninety to 180 minutes after plating, hepatocytes were washed and refed with medium containing 10 μCi radiolabeled thymidine. Seventeen to 20 hours after exposure to thymidine, coverslips bearing cultures were washed, fixed, and scored. All coded slides were read without knowledge of treatment group. Fifty nuclei were scored from each of three replicate cultures for a total of 150 nuclei from each rat.

Results and Discussion	All animals appeared normal following dose administration prior to harvest. For each treatment slide, the net nuclear counts were averaged and the mean ± standard deviation reported. 2-4 hour post dose harvest: The mean net nuclear grain count for the negative control group was -0.1. The means of the net nuclear grain counts for the 0.5, 1.0, and 2.0 g/kg bw treatment were -2.3, -2.4, and -2.9, respectively. The mean net nuclear grain count for he positive control group was 9.0. None of the test article doses caused a significant increase in the mean net nuclear counts compared to the negative control group. 12-16 hour post dose harvest: The mean net nuclear grain count for the negative control group was -3.5. The means of the net nuclear grain counts for the 0.5, 1.0, and 2.0 g/kg bw treatment were -2.4, -3.3, and -2.4, respectively. The mean net nuclear grain count for he positive control group was 8.7. None of the test article doses caused a significant increase in the mean net nuclear counts compared to the negative control group.
Conclusion	All criteria for a valid study were met. The results of the unscheduled DNA synthesis test with mammalian liver cells *in vivo* indicate that, under the test conditions, the test article did not induce a significant increase in the mean number of net nuclear grain counts (i.e., an increase of at least 5 counts over the negative control).
Klimisch criterium	1

[4.6] Oral Teratology Study

Study Title	Oral Teratology Study in Rats
Date	October 17, 1984
Test Facility	International Research and Development Corporation Mattawan, MI USA
GLP Compliance	Yes
Test Material	Sodium Octanoyloxybenzene Sulfonate (C8 AOBS)
Animal Species	Sprague-Dawley Rats. Females were 80 to 120 days of age, nulliparous, sexually mature and a minimum of 220 grams at study initiation. Males were sexually mature, healthy, gross normal in appearance.
Number of Animals	25 female rats /group ; 4 groups
Dosing	Doses of 0 (water vehicle control), 500, 1000, or 1500 mg/kg/day administered by oral gavage on gestation days 6 through 15. Dosing volume was 10 ml/kg.
Observations	Dams were checked daily for mortality and clinical signs of toxicity. Body weights and food consumption were recorded on gestation days 0, 6, 9, 12, 16 and 20. On gestation day 20, rats were sacrificed and examined macroscopically. Ovaries and uterine horns were examined for number of copora lutea, number and distribution of live young, number and distribution of fetal deaths or resorptions. Litter weights were recorded. Fetuses were individually weighed, sexed, and examined for external malformations and variations. One half of the fetuses were placed in Bouin's solution for soft tissue examination using Wilson's sectioning technique. The remaining one half of fetuses were prepared and stained with Alizarin Red for skeletal examination.
Results and Discussion (continued)	No mortality was present in the 0, 500, or 1000 mg/kg day groups. Three dams dosed with 1500 mg/kg/day died on gestation 13 or 15. Necropsy observations of animals that died on study included reddened stomach mucosa and distended intestines. Clinical observations in the mid and surviving high dose groups included respiratory rales and wet matted haircoat or material in the facial, ventral and/or anogenital areas. There were no differences in gross necropsy findings of the treated and control dams.

Results and Discussion (continued)	Oral administration of C8/10 AOBS from gestation day 6 through 15 resulted in a depression in maternal body weight change at all dosage levels during the first two measured intervals of treatment (days 6 to 9 and 9 to 12) and only in the high dose group during the last treatment interval (days 12 to 16). Similarly, mean food consumption was slightly decreased in the mid and high dose groups only during the treatment period. There were no indications of a treatment related effect on fetal or embryonic growth or survival. Ovulation, implantation, intrauterine development, and embryogenesis were uniform in all study groups. Similarly, the occurrence of malformations and developmental variations was not different in the treated groups relative to the control group. One nonviable fetus was observed in the 1000 mg/kg goup and one litter each in the control, 1000, and 1500 mg/kg groups had a single late resorption. Anomalies including vertebral anomalies with or without rib anomalies, microphthalmia, anophthalmia, sternoschisis, gastroschisis diaphragmatic hernia were noted occasionally in the control and mid dose groups. No malformed fetuses were present at the low and high dose levels.
Conclusion	When administered orally to pregnant Charles River CD rats on gestation days 6 through 15, C8/10 AOBS did not induce a teratogenic effect at dosage levels of 500, 1000, or 1500 mg/kg/day. The fetal NOEL was 1500 mg/kg/day and maternal NOAEL was 500 mg/kg/day.
Klimisch criterium	1

[4.7] Fertility Study

Study Title	Fertility Study in Rats
Date	March 28, 1986
Test Facility	International Research and Development Corporation Mattawan, MI USA
GLP Compliance	Yes
Test Material	Nonanoyloxybenzene Sulfonate (C9 AOBS)
Animal Species	Sprague-Dawley Rats
Number of Animals	38 rats /sex/group ; 4 dose groups; termination at gestation day 13 (for uterine examination group) or lactation day 21.
Dosing	Doses of 0, 100, 500, or 1000 mg/kg/day in deionized water (dosing volume of 5ml/kg) administered by oral gavage for 70 days prior to initiation of mating until termination, on either gestation day 13 or lactation day 21. F1 offspring were potentially exposed in utero and/or as neonates during lactation but did not directly receive the test article.
Observations	Estrous cycle determined in females 10 days prior to mating until the end of the mating period. Body weights and food consumption were recorded weekly until copulation, gestation days (GD) 0, 7, 13, and 20 and lactation days 0, 7, 14, and 21 for appropriate groups. Animals observed daily for clinical signs of toxicity, changes in appearance, behavior and mortality. Uterine exam group (GD13) - Ovaries and uterine horns examined for number of copora lutea, number of implantations, number and distribution of viable and nonviable fetuses, and early resorptions. Delivered litters - Litter size, number of still births, number of live births, and gross anomalies were determined. On postnatal day 4, litters were culled to 10 pups to achieve homogenous group size for evaluation of nursing, survival and body weight. Pups weighed on postnatal day 0, 4, 7, 14, and 21. Tissues and organs from all F0 animals were macroscopically observed, with special attention to reproductive organs, and preserved in 10% neutral buffered formalin for potential microscopic evaluation.

Results and Discussion (continued)	There were no treatment related differences in the estrous cycle of female rats. Mortality occurred in 1, 1, 2, and 10 rats in the 0, 100, 500, and 1000 mg/kg day groups, respectively. Macroscopic observations noted in three females that died on study included gastric lesions with thickened tissue indicative of mild gastric irritation. Five males that died in the high dose group had pulmonary lesions suggestive of pneumonia. Test articles was not directly implicated in the deaths. Clinical observations in the mid and high dose groups included excessive salivation and respiratory rales. There were no significant adverse effect on body weights or food consumption. The high dose males showed a slight yet consistent decrease in body weights (4% or less decrease) compared to control animals throughout the study. Uterine exam observations show no difference in the number of viable embryos, postimplantation loss, total implantations or number of corpora lutea. F0 Delivery and F1 Litter Observations - There was no test article effect observed on male or female fertility indices, copulatory indices, gestation length, mean number of live/dead pups on day 0, pup survival to weaning or pup body weight throughout lactation. There were no indications of a treatment related effect on fetal or embryonic growth or survival. Ovulation, implantation, intrauterine development, and embryogenesis were uniform in all study groups.
Conclusion	NOBS administered orally at dosage levels of 100, 500, or 1000 mg/kg/day did not result in adverse effects on fertility, parturition, neonatal viability, growth of the newborn or reproductive performance in rats. The NOEL and NOAEL were 1,000 and 100 mg/kg/day for reproductive and systemic effects, respectively.
Klimisch criterium	1

[4.8] 13 Week Oral (Dietary Administration) Toxicity Study

Study Title	P1407.02: 13 Week Oral (Dietary Administration) Toxicity Study in the Rat
Date	November 1984
Test Facility	Hazelton Laboratories North Yorkshire, ENGLAND
GLP Compliance	Yes
Test Material	Sodium Octanoyloxybenzene Sulfonate (C8 AOBS)
Animal Species	Rat, Sprague-Dawley
Number of Animals	40 rats /group (20 males, 20 females); 4 groups Animals were received at approximately 28 days of age with treatment beginning on approximately 42 days of age.
Dosing	Dietary levels of 0, 0.001, 0.01 and 0.1% (equivalent to 0, 10, 100, or 1000 mg/kg/day) were administered for 13 weeks. Concentration levels were adjusted to provide a constant dose level in relation to increasing body weight.

Observations	Animals were observed daily for overt signs of toxicity and mortality and weekly for systemic effects. Body weight and food consumption were recorded weekly throughout the study. Clinical laboratory studies were performed on blood and urine collected at weeks 12 and 13 and included hematology, blood chemistry and urinalysis. <u>Clinical chemistry</u> assessment included the following parameters: glutamate oxaloacetate transaminase (GOT) glutamate pyruvate transaminase (GPT) alkaline phosphastase blood urea nitrogen glucose sodium potassium calcium inorganic phosphate chloride total bilirubin creatinine total protein albumin albumin/globulin ratio <u>Hematology assessment</u> performed on blood taken into EDTA anticoagulant included the following parameters: hemoglobin mean cell volume red blood cell count total and differential white blood cell count platelets

	Urine analysis included the following parameters: pH volume specific gravity protein hemoglobin glucose ketones bilirubin urobilinogen reducing substances microscopy of centrifuged deposits including epithelial cell count Histology - Samples of the following tissues from all animals were preserved in 10% neutral buffered formalin: adrenals aorta brain (3 sections) caecum colon duodenum epididymides eyes femur with articular surface heart jejunum ileum lachrymal gland kidneys mammary gland liver esophagus lungs pancreas mesenteric lymph node prostate/uterus ovaries/testes salivary gland pituitary skeletal muscle rectum sternum sciatic nerves thymus seminal vesicles trachea spinal cord (3 levels) stomach spleen thyroid urinary bladder Opthalmoscopic examinations were performed on all animals in the control and high dose group prior to start of treatment and at study end. Complete necropsies were performed on all animals. The following tissues were weighed and fixed: adrenals, heart, pituitary, brain, kidney spleen, testes/ovaries, liver and thyroid. With the exception of the eyes, which were fixed in Davidson's solution, an extensive list of tissues as noted above were preserved in 10% neutral buffered formalin. All tissues from control and high dose animals, lung and liver tissue and gross lesions from low and intermediate dose groups were embedded, sectioned, stained and evaluated by a pathologist.

Results and Discussion	Administration of C8 AOBS did not result in any mortalities or induce any compound-related clinical signs of toxicity. There were no significant changes in body weights or food consumption. There were no toxicologically significant treatment related effects in the hematology, clinical chemistry or urine analysis parameters. Statistically significant increases were observed between the control and high dose males for neutrophils, lymphocytes, and BUN levels. In addition creatinine and sodium were statistically significant for the females. However, these changes were within the normal ranges observed in background data compiled at the laboratory. There were no treatment related effects on absolute or relative organ weights. Test article diet preparations were stable, homogeneous and formulated correctly. No treatment-related gross pathological findings or histopathological changes were observed in test animals compared to controls.
Conclusion	The study established 0.11% in diet (approximately 1,100 mg/kg/day) as the no observed adverse effect level (NOAEL). C8 AOBS was not considered to be systemically toxic up to a level of 1,110 mg/kg/day.
Klimisch criterium	1

BEYOND SIDS ENDPOINTS

[4.9] Primary Eye Irritation - Low Volume Eye Test Method

Study Title	Rabbit Eye Irritation (Low Volume Procedure)
Date	September 28, 1982
Test Facility	International Research and Development Corporation
GLP Compliance	Yes
Test Material	Sodium Nonanoyloxybenzene Sulfonate (NOBS)
Animal Species	New Zealand White Rabbits
Number of Animals	Group I - 6 rabbits (3 male, 3 female); Group II - 3 rabbits (1 male, 2 females

Dosing	Group I rabbits received 0.01 ml of test material (low volume procedure), placed directly on the cornea of one eye without rinsing (the eyelid was released immediately after instillation); Group II rabbits received 0.01 ml of test material directly on the cornea with rinsing (approximately 4 seconds after application using 20 ml of water).
Observations	Eyes were examined for corneal opacity, iritis and conjunctivitis and scored according to the methods of Draize (1959).
Results and Discussion	Group I (unrinsed eye) yielded a maximum average score of 33.7 (Day 2). Corneal involvement and iridal effects were observed in 6 of 6 animals at day 1. Conjunctival irritation ranged from mild to severe. All effects observed were reversible and animals returned to normal (1 animal in 3 days, 1 in 4 days, 3 in 7 days and 1 in 14 days). Group II (rinsed eyes) yielded a maximum average score of 20(Day 1). Effects noted include mild corneal involvement 1 animal, mild iridal effects and mild to severe conjunctival irritation. Eyes of all subjects returned to normal within 3-7 days (2 animals in 3 days and 1 in 7 days).
Conclusions	The test substance caused moderate irritation in all eyes, which cleared by Day 7, except for one eye, which cleared by Day 14 (unrinsed).
Klimisch criterium	1

[4.10] Primary Eye Irritation

Study Title	Rabbit Eye Irritation
Date	October 1, 1982
Test Facility	International Research and Development Corporation
GLP Compliance	Yes
Test Material	Sodium Nonanoyloxybenzene Sulfonate (NOBS)
Animal Species	Rabbits, New Zealand White
Number of Animals	Group I - 3 rabbits (2 male, 1 female); Group II - 3 rabbits (2 male, 1 females); Group III - 3 rabbits (1 male, 2 females)
Dosing	Group I rabbits received 3 mg of test material in their right eye (conjunctival sac) without rinsing (eyelid was gently held closed for approximately one second after instillation); Group II rabbits received 3 mg of test material in the conjunctival sac followed by rinsing (approximately 4 seconds after application using 20 ml of water); and Group III rabbits received 0.1 ml per test eye as a 10% w/v solution in the conjunctival sac (eye held closed for approximately 1 sec) without rinsing.
Observations	Eyes were examined for corneal opacity, iritis and conjunctivitis and scored according to the methods of Draize (1959).
Results and Discussion	Group I - (unrinsed) - yielded a maximum average score of 16.7 (Day 1). Corneal involvement was observed in 2 of 3 animals and mild iridal effects. Mild to moderate conjunctival redness and mild swelling was also noted. All effects observed cleared within 4 days (2 animals in 3 days, 1 in 4 days). Group II - (rinsed)- yielded a maximum average score of 5.3 (Day 1). No effects on the corneal. Mild iritis and conjunctivitis was transient and cleared in all 3 animals within 2 days. Group III - (unrinsed) yielded a maximum average score of 28.0 (Day 1). Corneal involvement, mild iritis, and mild to severe conjunctival irritation was observed in all animals. All effects were reversible (2 animals in 4 days and 1 in 21 days).

Conclusion	The test substance caused slight to moderate irritation in all eyes, which cleared by Day 4 (unrinsed), except in the 10% w/v unrinsed group, which cleared by Day 21.
Klimisch criterium	1

[4.11] Primary Skin Irritation

Study Title	Rabbit Skin Irritation (Department of Transportation -DOTP method)
Date	December 13, 1982 (Study I) October 12, 1983 (Study II)
Test Facility	Miami Valley Laboratories, Procter & Gamble Cincinnati, OH USA
GLP Compliance	Yes
Test Material	Sodium Nonanoyloxybenzene Sulfonate (NOBS, administered as a 40% w/v aqueous suspension or a moistened paste)
Animal Species	New Zealand White Rabbits
Number of Animals	Study I - 6 rabbits (5 males, 1 female); Study II - 6 rabbits (3 males, 3 females)
Dosing	Study I - 0.5 ml of the test material (40% w/v suspension in distilled water) was applied to 1 x1 inch gauze patches and occluded for 4 hours on intact, unabraded skin. Study II - 0.5 g of undiluted test material, slightly moistened with 0.9% saline was applied to 1 x 1 inch gauze patches and occluded for 4 hours on intact unabraded skin.
Observations	After 4 hours of exposure, the patches were removed from animals in both studies and the application sites were observed for irritation and corrosion. Readings were made again at the end of 48 hours.
Results and Discussion	Study I - The average dermal irritation scores for animals at 4 hours were 0.54 and 0 for erythema and edema, respectively; whereas at 48 hours the scores were 1.3 and 0 for erythema and edema, respectively. The primary dermal irritation index was calculated to be 0.9, which translated to a slight irritant. Study II - The average dermal irritation scores for animals at 4 and 48 hours were 0 for erythema and edema.
Conclusion	Dilute and undiluted test material was non-irritating and noncorrosive to skin .
Klimisch criterium	1

[4.12] Delayed Contact Hypersensitivity in Guinea Pigs

Study Title	Delayed Contact Hypersensitivity Study in Guinea Pigs (Modified Buehler Method)
Date	October 6, 1982
Test Facility	Miami Valley Laboratories, Procter & Gamble Cincinnati, OH USA
GLP Compliance	Yes
Test Material	Sodium Nonanoyloxybenzene Sulfonate (NOBS)
Animal Species	Guinea Pig (Hartley Albino)
Number of Animals	Test = 20 (10 male, 10 female); Control = 10 (5 male, 5 female)
Dosing	Based on previous skin irritation information for a similar compound, a concentration of 20% aqueous solution (w/v) was used for the three week induction. A screening study was conducted to determine the highest non irritating concentration for challenge. Based on the results, a 20% (w/v) aqueous solution was used as the challenge concentration.
Observations	The test sites were graded for skin responses, including erythema and edema, using a standardized scoring scale at 24 and 48 hours following chamber application at induction. Following the challenge dose, the skin was depilated after 19 hours and at 24 and 48 hours post challenge, depilated animals were scored for erythema severity using a 0-3 scale (0 = no reaction, ± = slight patchy erythema, 1= slight, but confluent or moderate, patchy erythema, 2= moderate erythema, 3= severe erythema with or without edema).
Results and Discussion	Dermal scores of 0 or +/- were observed in all test and control animals. No evidence of skin sensitization was observed.
Conclusion	The test material is not a dermal sensitizer under the conditions of this test.
Klimisch criterium	1

[4.13] Dermal Sensitization in Guinea Pigs - Modified Buehler

Study Title	Delayed Contact Hypersensitivity Study in Guinea Pigs (Modified Buehler Method)
Date	March 12, 1986
Test Facility	Hill Top Research, Inc.
GLP Compliance	Yes
Test Material	Sodium Nonanoyloxybenzene Sulfonate (NOBS)
Animal Species	Guinea Pig (Hartley Albino)
Number of Animals	Test = 20 (10 male, 10 female); Control = 10 (5 male, 5 female), Rechallenge naïve control = 10 (5 male, 5 female)
Dosing	Based on skin irritation screening information, a concentration of 5% in distilled water (w/v) was used for the three week induction (one six hour patch per week). The concentration used for the challenge phase of the study was 2.5% . Test animals were rechallenged and a naïve control group was dosed with a 1% solution of test material in distilled water for six hours.
Observations	The test sites were graded for skin responses, including erythema and edema, at 24 and 48 hours following patch removal. The procedure for grading the skin after the irritation screen and challenge dose included depilatingthe skin after 19 hours and grading at 24 and 48 hours post challenge. For rechallenge, skin was graded at 24 and 44 hours, depilated, and graded again at 48 hours. The standardized scoring scale assessed severity of erythema using a 0-3 scale (0 = no reaction, ± = slight patchy erythema, 1= slight, but confluent or moderate, patchy erythema, 2= moderate erythema, 3= severe erythema with or without edema).
Results and Discussion	Following the primary challenge, 6/20 and 0/10 animals produced dermal scores greater than +/- at 24 and/or 48 hours in test and control animals, respectively. A rechallenge was conducted using a 1% test material in distilled water. The grades for skin response demonstrated 2/20 test animals and 0/10 control animals responded with a score greater than +/- at 24 and/or 48 hours.
Conclusion	These data indicate a contact sensitization response occurred in some of the test animals at the concentrations tested.
Klimisch criterium	1

[4.14] Dermal Sensitization in Guinea Pigs - Modified Buehler

Study Title	A Dermal Sensitization Study in Guinea Pigs-Modified Buehler Design
Date	September, 2000
Test Facility	Procter & Gamble Non-Clinical Testing Laboratory (PGNCTL) Cincinnati, OH
GLP Compliance	Yes
Test Material	Sodium Nonanoyloxybenzene Sulfonate (NOBS extrudate: 78% C9 AOBS)
Animal Species	Guinea Pig (Hartley Albino)
Number of Animals	Test = 20 (10 male, 10 female); Control = 10 (5 male, 5 female) Induction range finder = 4 animals, Challenge range finder = 8 animals.
Dosing	Appropriate concentrations were chosen based on the range finding studies. For induction, 0.3 ml of 10% test material in reverse osmosis water was applied for 6 hours under an occlusive Hilltop patch once per week for three consecutive weeks. Following a two week rest period, challenge phase was conducted under similar conditions at 0.5%.
Observations	The test sites were graded for skin responses, including erythema and edema, using a standardized scoring scale at 24 and 48 hours following chamber application at induction. During challenge, the test sites were graded through hair at 19 hours and then following depilation at 24 and 48 hours after patch removal.
Results and Discussion	Irritation was noted during induction. At the 24 and 48 hr scoring intervals during challenge, dermal score of 1 was noted in 1/20 and 0/10 test and challenge control animals, respectively. All other scores ranged from 0 to ± in all other test and control animals. No evidence of sensitization was observed in guinea pigs exposed to the test material. The results show a response in 1/20 test subjects, which does not equate to a positive response.
Conclusion	The test material is not a dermal sensitizer under the conditions of this study according to global guidelines..
Klimisch criterium	1

[4.15] Local Lymph Node Assay

Study Title	Murine Local Lymph Node Assay
Date	September, 2000
Test Facility	Procter & Gamble Non-Clinical Testing Laboratory (PGNCTL) Cincinnati, OH
GLP Compliance	Yes
Test Material	Sodium Nonanoyloxybenzene Sulfonate (NOBS extrudate: 78% C9 AOBS)
Animal Species	Mice
Number of Animals	5 mice/group 4 dose groups, vehicle control (reverse osmosis water), naïve control
Dosing	For each treatment group, five mice were treated daily for three consecutive days by direct epicutaneous application of 25 µl of test article to each ear. In addition a vehicle control (reverse osmosis water) and a naïve control (no treatment) were evaluated. Approximately 71 hours after final test application, mice were injected i.v. in the tail vain with tritiated thymidine to label proliferating cells.
Observations	Mice were observed immediately prior to and approximately 2-4 hours after dosing for any significant alterations in appearance of the application site. Mice were observed twice daily for general health and mortality. Five hours after injection, lymph nodes were harvested and single cell suspensions prepared and quantitated by liquid scintillation spectrometry.
Results and Discussion	All animals appeared normal throughout the study. Body weight gain was noted for all treatment animals during the day -1 and day 6 interval. The stimulation indices of lymph nodes were calculated for each treatment group compared to controls. The groups treated with 10%, 5.0%, 1.0% and 0.5% demonstrated stimulation indices of 0.5, 0.6, 0.9, and 0.7, respectively. A stimulation index of 3.0 (three fold increase over controls) would be considered a positive immunological response for sensitization.
Conclusion	Treatment with the test article did not result in an increase in lymph node proliferation compared to controls demonstrating the test material is not a dermal contact allergen.
Klimisch criterium	1

[4.16] 28 Day Subchronic Percutaneous Toxicity Study

Study Title	28 Day Subchronic Percutaneous Toxicity Study in Rabbits
Date	October 22, 1982
Test Facility	Springborn Life Sciences Laboratories, Inc. Spencerville, OH USA
GLP Compliance	Yes
Test Material	Sodium Octanoyloxybenzene Sulfonate (C8 AOBS) 50% Sodium Decanoyloxybenzene Sulfonate (C10 AOBS) 50%
Animal Species	New Zealand White Rabbits weighing between 2.0 - 3.0 kg.
Number of Animals	10 rabbits/group (5 males, 5 females); 2 treatment groups and 1 control
Dosing	Water vehicle control, 1.5% or 20% C8/10 AOBS in water (2 ml/kg dosing volume). Dosing on abraded skin for 7 hours/day, 5 days/week for 4 weeks. All test sites are washed with tepid water approximately 7 hours after application.

Observations	Animals were observed daily for overt signs of toxicity, mortality and the skin was graded each day of dosing. Body weights were recorded weekly. At necropsy, liver and kidneys were weighed and a hematological assessment including hemoglobin, hematocrit, white blood cell count, red blood cell count, mean corpuscular volume, mean corpuscular hemoglobin, and differential white blood cell count determined for each animal. All animals were necropsied and gross observations recorded. Tissues listed below were taken at the end of the study for microscopic evaluation. Organ weights were recorded for the liver and kidneys. Histology - A sample of the following tissues were collected, preserved in 10% neutral buffered formalin and examined microscopically: Lung — Heart Aorta — Tongue Trachea, esophagus, thyroid — Submandibular lymph node Ileocecocolic lymph node — Stomach Liver — Gall bladder Duodenum — Jejunum Ileum — Cecum, colon Urinary bladder — Kidneys Prostate & seminal vesicle — Testis & epididymis Ovaries, vagina, uterine horns — Adrenals Thymus — Psoas muscle Spleen — Pancreas Bone — Skin (test site) Brain — Lumbar spinal cord Sciatic nerve — Submandibular salivary gland Pituitary gland — Eyes Gross lesions
Results and Discussion	No mortalities or clinical signs of toxicity occurred except for diarrhea and soft stools (also in control group). There were no changes in body weights, food consumption, ophthalmoscopy, hematology, absolute or relative organ weights or effects in the macroscopic and microscopic pathology, except for skin. Skin responses at the test site, both gross and microscopic, increased with the concentration of test article. Slight erythema and desquamation were observed in the 1.5% group. Exposure to 20% caused slight erythema, edema and desquamation and slight to moderate atonia and fissuring. The microscopic evaluation of the skin from this group revealed dermal effects, which included inflammation, parakeratosis, acanthosis, hyperkeratosis, and vesiculation.

Conclusion	The application of test material at levels up to 20% (0.4 g/kg/day) to the abraded skin of rabbits did not cause any detectable systemic toxicity. The effects of C8/10 AOBS appears to be limited to dermal irritation and microscopic changes at the application site when applied to the skin up to 20% w/v and dosed 5 days/week for 4 weeks. The degree of irritation appears to be dose related.
Klimisch criterium	1

[4.17] Absorption, distribution, metabolism, and excretion (ADME) study

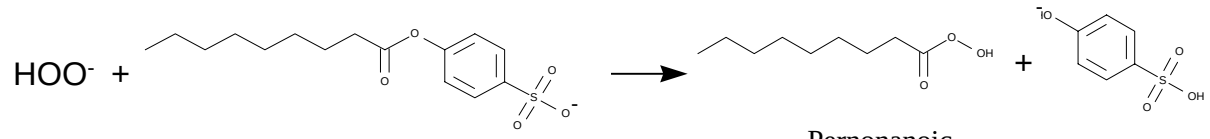
Study Title	The absorption, distribution, metabolism, and excretion of nonanoyloxybenzene sulfonate after oral or dermal dosing
Date	July 15, 1983
Test Facility	Procter & Gamble Company, Miami Valley Laboratories
GLP Compliance	Yes
Test Material	^{14}C Nonanoyloxybenzene Sulfonate (NOBS) - (uniformly ring labeled) The radiochemical purity of the test material was 97%.
Animal Species	Sprague Dawley Rats
Number of Animals	4 male rats/group, each male weighing between 175-225 grams
Dosing	Animals are food-fasted overnight before dosing and for four hours after dosing. Radiolabeled test material was administered by the following exposure routes at a dosage of 10 mg/kg: Oral gavage alone and with bile duct canulation- Vehicle was distilled water with concentration of test material at ~2.0 mg/g (5-10 μCi/g) Dermal - Vehicle was distilled water with concentration of test material at ~20 mg/g (50-100 μCi/g). Approximately 0.1g solution applied.
Observations	Fecal and urine samples were collected at 24, 48 and 72 hours after dosing. Carbon dioxide samples were collected at 8 hour intervals for 72 hours. At the end of the test period, the cage was washed with 0.1N HCl. At necropsy the following tissues and samples were collected and analyzed for radioactivity: Urine, feces, CO2, blood, plasma, liver, kidney, testes, heart, lung, spleen, pancreas, brain, bone marrow, muscle (hink limb), bone (femur), adipose (at the psoas), GI tract, GI tract wash, carcass, cage wash.

Results and Discussion	The dermal ADME study showed there was no significant absorption by this route of exposure. Less than 1% was absorbed with 0.56 ± 0.18% eliminated from urine, < 0.02% via CO2, and < 0.16% via faeces after 72 hours. Recovery from the skin application site and the cage wash was 99.1 ± 1.0% and 0.14 ± 0.06%, respectively. Total recovery was 101.9 ± 0.7%. NOBS was rapidly absorbed and eliminated in the oral (gavage) ADME study. Essentially all of the oral dose was eliminated in 72 hours; 80.2 ± 8% via urine, 1.6 ± 0.1% via faeces, and < 0.22% via CO2, and 19.7 ± 6.1% via the cage wash. At 72 hours after dosing, there was no concentration of the 14C-labelled material in any of the tissues examined including reproductive tissues. Bile duct canulation showed enterohepatic circulation did not occur. Total recovery was 101.8 ± 3.3%. HPLC analysis of the urine showed that no parent compound was excreted. Approximately 99% of the radioactivity in the urine represented a single metabolite consistent in HPLC retention time with hydroxybenzene sulphonate (phenol sulphonate).
Conclusion	These ADME data indicate that NOBS is very poorly absorbed upon dermal exposure (the most relevant route of exposure) and highly absorbed following oral exposure. Absorbed material appears to be rapidly metabolised (via cleavage of the ester linkage) with excretion of the phenol sulphonate moiety and assumed normal catabolism of the fatty acid moiety via the established odd-chain fatty acid pattern (AL Lehninger, Biochemistry, 2nd edition, 1975, chapter 20, p.555).
Klimisch criterium	1

APPENDIX B: Degradation of NOBS in the wash solution [1]

A. Perhydrolysis - major pathway

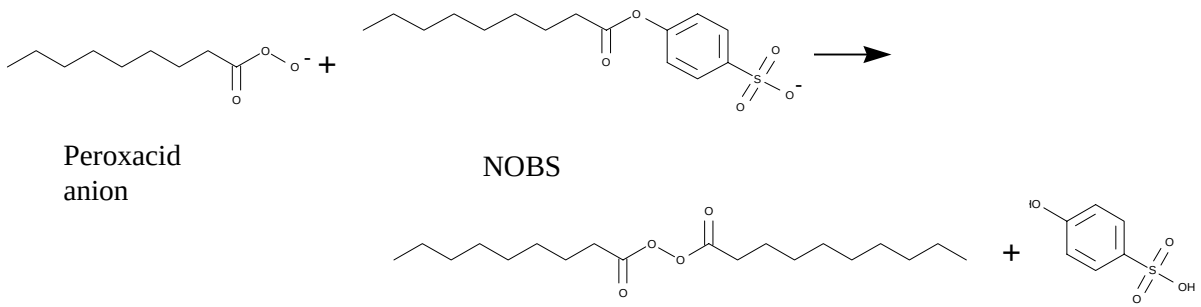
Perhydrolysis is the desired and favored reaction under wash conditions. Under the temperature and pH conditions created by the detergent formula in the wash solution, sodium perborate monohydrate releases hydrogen peroxide that reacts with NOBS to form the peroxy acid, pernonanoic acid, and at the same time releases phenol sulfonate. These reactions are largely complete within the first two minutes of the wash.



Peroxide anion | NOBS | Pernonanoic acid | Phenol Sulfonate

B. Diacylperoxide formation - minor pathway

Detergent formulations containing NOBS are designed to minimize diacyl peroxide formation. Like the peroxide anion, pernonanoic acid can also react with the electrophilic carbonyl carbon of NOBS to form a diacylperoxide. Since diacylperoxide is a less efficient bleach than the peroxy acid, laundry detergents are designed to adjust several conditions in the wash solution to minimize its formation.



Peroxacid anion | NOBS | Diacylperoxide | Phenol Sulfonate

[1] Degradation data on a similar ingredient were published in: Calvin GC (1992) Risk management case history - Detergents. In: Richardson ML (ed) Risk management of chemicals. ISBN 0-85186-467-8. pp: 120-136.

C. Hydrolysis - minor pathway

Detergent formulations containing NOBS are designed to minimize alkaline hydrolysis of the ester bond in NOBS. This reaction can be catalyzed by the hydroxyl ion released from perborate and result in formation of the nonanoic acid and phenol sulfonate. Since neither of these products possess bleaching, sanitizing or other properties beneficial to detergent performance, hydrolysis of NOBS detracts from the efficacy of NOBS.

The *n*-pernonanoic acid is the major bleaching species so the perhydrolysis is the favored reaction. The rate of perhydrolysis is much greater than the rate of hydrolysis because the reaction with the peroxy anion (HOO^-) is approximately 150-fold faster than that with the hydroxyl ion (HO^-) with carbon centered electrophiles. This minimizes the hydrolysis reaction in the wash. The rate of diacylperoxide formation is a function of wash temperature, pH and perborate concentration. Formation of this less efficient bleach is minimized (<10%) by keeping the pH near 10 using sodium carbonate and providing an excess perborate relative to NOBS. Thus, the perhydrolysis reaction predominates.

D. Relative stability of NOBS and pernonanoic acid

1. Dry conditions

Under dry conditions, for example, in the dry detergent granules, the pernonanoic acid will not be present. NOBS will be present and is quite stable.

2. Wet conditions

As soon as the detergent granules are added to the wash water, the reactions described above will be initiated. Under wet conditions, perhydrolysis rapidly occurs and NOBS has a half-life of about 15-30 seconds. The half-life of the pernonanoic bleach is also relatively short depending on the amount of soil in the laundry. Based on consumer data of average soil load in a wash and timed trials, over 90% of the pernonanoic acid bleach is consumed during the first 8 minutes of the wash cycle. Following completion of the wash cycle, wash water would normally be released into the sewer system and a POTW for treatment.

E. Analytical data on degradation of NOBS in wash solution

In the experiment described below, the degradation of NOBS was determined in a detergent solution at 1%, reflecting a typical use concentration washing.

1. Methodology

NOBS concentration:	1% aqueous detergent solution
Time-points:	0, 1, 3 and 5 minutes
Temperature:	40^{o}C
Product:	US detergent with bleach

INGREDIENT	%

SURFACTANTS	
Anionic surfactants	18.25
Nonionic surfactant	1.43
BUILDERS	40.54
BLEACH	
Perborate-monohydrate	2.23
NOBS	1.92
Others	0.49
ENZYMES	0.26
MISCELLANEOUS	
Sodium sulfate	17.48
Others	4.43
PERFUME	0.23

Ten grams of detergent was added to 1 liter of water stirred in a Sotax at 150rpm. Aliquots of 1ml were taken from this solution after 1, 3, or 5 minutes, quenched with acidified water and analyzed by HPLC.

2. Results

The table below presents the concentration of residual NOBS in a wash solution 1 to 5 minutes after the start of a wash cycle.

Time (min)	% of initial
Initial	100.0
1	9.4
3	nd (i.e., < 1%)
5	nd(i.e., < 1%)

3. Conclusion

The degradation of NOBS at 40^{o}C in a 1% aqueous solution of laundry detergent is extremely fast: after 3 minutes, NOBS could no longer be detected.

APPENDIX C: Comparison of P&G to E-FAST Exposure Estimates

To provide a basis for understanding how the results of an assessment conducted by the US EPA for consumer exposure might differ from the P&G assessment, the **E-FAST** model (Exposure and Fate Assessment Screening Tool) was used to evaluate the consumer exposure to NOBS. E-FAST was developed by Versar, Inc. for U.S. EPA's Office of Pollution Prevention, Economics, Exposure and Technology Division. E-FAST provides screening level estimates of concentrations of chemicals released to air, surface water, landfills, and from consumer products and can estimate potential dermal, inhalation and ingestion rates resulting from these releases. Modeled estimates of concentrations and doses are designed to provide high end to bounding estimates of exposure for use in screening level assessments. Information about E-FAST is available via OPPT's Exposure Assessment Tools and Models Web site: www.epa.gov/opptintr/exposure.

NOBS is used in P&G granular and tablet laundry detergents, however, E-FAST does not contain data for estimating exposure from use of a granular laundry detergent; therefore, E-FAST's Liquid Laundry Detergent scenario was used. As discussed in [3.4], the most likely scenarios for consumer exposure to NOBS are skin contact during hand laundering and during use of a concentrated paste for pretreatment of fabric.

Overview of Differences in Assessment Approaches

In conducting these exposure calculations using E-FAST, it must be recognized that there are inherent differences in the ways that the exposure parameters are expressed in E-FAST compared to those in the P&G assessment described in the previous section. For example, rather than using a use concentration of consumer product, E-FAST uses a factor representing the amount retained on skin which is equal to the thickness of the product film on the skin times the dilution fraction of the product in water times the product density. For example, for NOBS hand laundering, the amount retained on skin would be 1.1 x 10-5 g/cm2 (i.e., 0.005 cm thickness of a liquid laundry detergent product film on skin (E-FAST default) times 0.002 dilution fraction for a liquid laundry detergent (E-FAST default) times1.1 g/cm3 for granule product density). Also rather than using a factor representing the area of exposed skin, E-FAST uses a surface area to body weight value. For example for NOBS hand laundering, E-FAST would use 15.6 cm2/kg (i.e., 1,120 cm2 which is the median value for the surface area of hands (E-FAST default) divided by a body weight of 71.8 kg (E-FAST default)).

One major difference between the P&G and the E-FAST exposure calculations is that where available, P&G incorporates a dermal absorption fraction, which for NOBS is 1%. The percent dermal absorption represents the fraction of NOBS that will penetrate the skin and thus the internal dose. However, E-FAST does not allow for the use of a dermal absorption fraction. Therefore, the effect of a dermal absorption fraction less than 100% needs to be calculated by hand from the E-FAST results.

Comparison of Default Values

A comparison of the default values used in the P&G and E-FAST dermal exposure assessments for hand laundry and some of the intermediate calculated values are presented in Table 1.

Table 1. Comparison of Exposure Factors used in P&G and E-FAST exposure calculations for Hand Laundry Scenario

Parameter	EPA default or calculated value	P&G default or calculated value
Frequency of Use -- FQ	52/yr = 0.14/day	0.38/day
Film thickness - FT	0.005 cm	0.0024 cm
Dilution factor - DF	0.002	
Use concentration of product - PC		5 mg/ml
Product density - PD	1.1 g/cm^3	1.1 g/cm^3
Weight Fraction of NOBS in Product - WF	0.06	0.06
Amount Retained on Skin -AQ	1.1 x 10^{-5} g/cm^2-event	1.2 x 10^{-5} g/cm^2 - event (calc)
Body weight - BW	71.8 kg	70 kg
SA/BW ratio	15.6 cm^2/kg	27.1 cm^2/kg (calc)
Surface area exposed – SA [(a)]	1,120 cm^2 (calc)	1,900 cm^2
Concentration of NOBS in solution -- Q	0.00013 g/cm^3 (calc)	0.0003 g/cm^3 (calc)
Amount of solution on skin -- SQ	5.6 cm^3 (calc)	4.56 cm^3 (calc)

[(a)] EPA assumes that hands are exposed and P&G assumes that both hands and forearms are exposed.

Table 2 gives the same comparison for the pre-treatment scenario. However since there is no default pretreatment scenario in E-FAST the exposure factors were entered in the user-defined scenario option. For this reason, many of the parameters entered are consistent with those in the P&G scenario.

Table 2. Comparison of Exposure Factors used in P&G and E-FAST exposure calculations for Pretreatment Scenario

Parameter	EPA default, user defined or calculated value	P&G default or calculated value
Frequency of Use -- FQ	1/day	1/day
Film thickness - FT	0.005 cm	0.0024 cm
Dilution factor - DF	1	1

Use concentration of product - PC	.55 g/cm^3	1.1g/cm^3
Product density - PD	1.1 g/cm^3	1.1 g/cm^3
Weight Fraction of NOBS in Product - WF	0.06	0.06
Amount Retained on Skin -AQ	0.0028 g/cm^2-event	0.0026 g/cm^2 - event (calc)
Body weight - BW	71.8 kg	70 kg
SA/BW ratio	3.9 cm^2/kg (calc)	2.8 cm^2/kg (calc)
Surface area exposed – SA [(a)]	280 cm^2	200 cm^2
Concentration of NOBS in solution -- Q	0.033 g/cm^3 (calc)	0.066 g/cm^3 (calc)
Amount of solution on skin -- SQ	1.4 cm^3 (calc)	0.48 cm^3 (calc)

[(a)] Both use 25% of hands are exposed.

Comparison of Exposure Assessment Results

For both exposure scenarios the respective equations used to calculate the external exposure are for EPA was Exposure (g/kg/day) = FQ x AQ x WF x SA/BW and for P&G was Exposure (g/kg/day) = FQ x Q x SQ / BW and where Q = PC x WF x 10^{-3} , AQ = FT x DF x PD or Q/WT x SQ / SA and SQ = FT x SA. The external exposure assessment results are compared in Table 3.

Table 3. Comparison of External Exposure Calculated by E-FAST and P&G.

Scenario	E-FAST	P&G
Hand Laundry	1.3 x 10^{-6} g/kg/day	7.5 x 10^{-6} g/kg/day
Pretreatment	6.6 x 10^{-4} g/kg/day	4.1 x 10^{-4} g/kg/day

The above estimates conservatively assume 100% absorption. When there is evidence to support less than 100% dermal penetration the resulting internal dose may be determined by multiplying the external exposure by a dermal penetration fraction. The ADME study found that NOBS was poorly absorbed (less than 1%). E-FAST does not allow for the use of a dermal absorption fraction. Therefore, this needs to be calculated by hand from the E-FAST results, and is shown in Table 11.

Table 4. Comparison of Internal Doses Calculated by E-FAST and P&G.

Scenario	E-FAST	P&G
Hand Laundry	1.3 x 10^{-8} g/kg/day	7.5 x 10^{-8} g/kg/day
Pretreatment	6.6 x 10^{-6} g/kg/day	4.1 x 10^{-6} g/kg/day

Conclusion: The consumer exposure estimates from the E-FAST runs are comparable in magnitude to those estimates derived from typical calculations developed by P&G. Both methods arrived at a external dermal exposure without consideration of dermal penetration of less than 0.01 mg/kg/day from hand laundering of fabrics and less than 1 mg/kg/day for pretreatment for a 6% NOBS granular laundry detergent. The resulting internal dose is less than 0.0001 mg/kg/day from hand laundering and less than 0.01 mg/kg/day for pretreatment. Using either method, the exposure estimates demonstrate very low potential for consumer exposure to NOBS from use of a granular laundry detergent.

APPENDIX D: Exposure Summaries

Outline A: Basic Chemical Manufacturing and Use Exposure-Related Information

I. Identification Information	
(1) Assessment Identification and Date	NOBS—October 2001
II. Scope	
(2) Activity	Chemical manufacture and use
(3) Coverage	Entire U.S.
III. Chemical information	
(4)Chemical Category	--
(5) Chemical Name (s)	Nonanoic acid, sulfophenyl ester, sodium salt (NOBS)
(6) CAS Number (s)	91125-43-8
(7) Other Constituents (If Applicable)	
(8) Physical Form	Extrudate (particles 500 - 1000 μm)
IV. Production, Import and Use	
(9) Estimated Volume	11,100 metric tons
(10) Function/Product Use Categories	Bleach activator in granular and tablet laundry detergents used by consumers (100%)
V. Potential Releases and Exposures	
(11) General description of Potential Releases and Exposures	Potential exposures include manufacturing and formulation plant workers, consumers and the environment.
(12) Discussion of Factors that Mitigate or Exacerbate Releases and Exposures	NOBS is produced in an enclosed, controlled release process. Low volatility and production as an extrudate minimizes potential for inhalation exposure by workers and consumers. Detergents containing NOBS are formulated in continuous operation, dedicated equipment systems, where no releases occur during regular production. For equipment clean-up, hot water is used and disposed via the drain to waste water treatment. Personal protective equipment further minimizes workplace exposure. In its intended use, NOBS is degraded (>99% in 3 minutes) during the laundry wash process, prior to wastewater disposal. Any residual NOBS is rapidly and completely biodegraded and highly removed during wastewater treatment (>95% removal), resulting in negligible aquatic and indirect exposure.
(13) Remarks	

Outline C: Modeling Evaluations

I. Identification Information	
(1) Assessment Identification and Date	NOBS—October 2001
(2)Chemical Category	--
(3) Chemical Name (s)	Nonanoic acid, sulfophenyl ester, sodium salt (NOBS)
(4) CAS Number (s)	91125-43-8
II. Modeling Objective	
(5) Modeling Study Objective	Estimate surface water concentration following consumer use, disposal and wastewater treatment.
III. Description of Model	
(6) Tool or Model	E-FAST-US EPA Screening Level Model
(7) Validation/Peer Review	
(8) Availability and Documentation	EPA Website http://www.epa.gov/opptintr/exposure/docs/efast.htm
IV. Description, Inputs and Results	
(9) Description of Modeled Scenario	Following consumer use in laundry detergents, unreacted NOBS is disposed to sewer and waste water treatment. This study models the concentration of unreacted, unremoved NOBS in surface waters.
(10) Exposure Medium Modeled	Aquatic
(11) Input parameters	Per capita water use is 364 l/cap.day, a US population of 2.5×10^8 (EPA defaults), 99% degradation of 11,100 t/y during the wash, no loss of NOBS in the sewage collection and conveyance system, a removal of 95% during waste water treatment
(12) Results	0.003 ng / l (50^{th} %) to 0.040 ng / l (10^{th} %)
(13) Reliability	Assessment conservatively assumes that neither hydrolysis nor perhydrolysis occurs in sewer conveyance system. Removal in wastewater treatment was conservatively assumed to be 95% vs 99+% observed in studies.
(14) Remarks	

Outline C: Modeling Evaluations

I. Identification Information	
(1) Assessment Identification and Date	NOBS—October 2001
(2)Chemical Category	--
(3) Chemical Name (s)	Nonanoic acid, sulfophenyl ester, sodium salt (NOBS)
(4) CAS Number (s)	91125-43-8
II. Modeling Objective	
(5) Modeling Study Objective	Estimate surface water concentration following manufacturing release and wastewater treatment. (Batesville, AK)
III. Description of Model	
(6) Tool or Model	E-FAST-US EPA Screening Level Model
(7) Validation/Peer Review	
(8) Availability and Documentation	EPA Website http://www.epa.gov/opptintr/exposure/docs/efast.htm
IV. Description, Inputs and Results	
(9) Description of Modeled Scenario	Manufacturing release due to cleaning and spillage is disposed to sewer and wastewater treatment. This study models the concentration of unremoved NOBS in surface waters.
(10) Exposure Medium Modeled	Aquatic
(11) Input parameters	335 days of operation on site, 0.15 % loss from equipment cleaning (e.g., wash down of the tower, scrubber water) and from spillage (U.S. EPA 1996), all the aqueous release goes to municipal waste water treatment before release to the environment.
(12) Results	16 μg / l
(13) Reliability	Assessment conservatively assumes that neither hydrolysis nor perhydrolysis occurs following discharge at the manufacturing site. Removal in wastewater treatment was conservatively assumed to be 95% vs 99+% observed in studies.
(14) Remarks	

Outline C: Modeling Evaluations

I. Identification Information	
(1) Assessment Identification and Date	NOBS—October 2001
(2)Chemical Category	--
(3) Chemical Name (s)	Nonanoic acid, sulfophenyl ester, sodium salt (NOBS)
(4) CAS Number (s)	91125-43-8
II. Modeling Objective	
(5) Modeling Study Objective	Estimate surface water concentration following formulation plant release and wastewater treatment. (Augusta, GA)
III. Description of Model	
(6) Tool or Model	E-FAST-US EPA Screening Level Model
(7) Validation/Peer Review	
(8) Availability and Documentation	EPA Website http://www.epa.gov/opptintr/exposure/docs/efast.htm
IV. Description, Inputs and Results	
(9) Description of Modeled Scenario	Formulation release due to cleaning and spillage is disposed to sewer and wastewater treatment. This study models the concentration of unremoved NOBS in surface waters.
(10) Exposure Medium Modeled	Aquatic
(11) Input parameters	Forty-five % of NOBS produced in the Eastman plant (i.e., 5,001 metric tons/y) is formulated in the Augusta plant.
(12) Results	0.23 μg / l (7Q10, 10^{th} %tile low flow)
(13) Reliability	Assessment conservatively assumes that neither hydrolysis nor perhydrolysis occurs following discharge at the processing site. Removal in wastewater treatment was conservatively assumed to be 95% vs 99+% observed in studies.
(14) Remarks	

Outline C: Modeling Evaluations

I. Identification Information	
(1) Assessment Identification and Date	NOBS—October 2001
(2)Chemical Category	--
(3) Chemical Name (s)	Nonanoic acid, sulfophenyl ester, sodium salt (NOBS)
(4) CAS Number (s)	91125-43-8
II. Modeling Objective	
(5) Modeling Study Objective	Estimate surface water concentration following formulation plant release and wastewater treatment. (Pineville, LA)
III. Description of Model	
(6) Tool or Model	E-FAST-US EPA Screening Level Model
(7) Validation/Peer Review	
(8) Availability and Documentation	EPA Website http://www.epa.gov/opptintr/exposure/docs/efast.htm
IV. Description, Inputs and Results	
(9) Description of Modeled Scenario	Formulation release due to cleaning and spillage is disposed to sewer and wastewater treatment. This study models the concentration of unremoved NOBS in surface waters.
(10) Exposure Medium Modeled	Aquatic
(11) Input parameters	Fifty-five % of NOBS produced in the Eastman plant (i.e., 6,112 metric tons/y) is formulated in the Alexandria/Pineville plant.
(12) Results	0.38 μg / l: (7Q10, 10^{th} %tile low flow)
(13) Reliability	Assessment conservatively assumes that neither hydrolysis nor perhydrolysis occurs following discharge at the processing site. Removal in wastewater treatment was conservatively assumed to be 95% vs 99+% observed in studies.
(14) Remarks	

Outline C: Modeling Evaluations

I. Identification Information	
(1) Assessment Identification and Date	NOBS—October 2001
(2)Chemical Category	--
(3) Chemical Name (s)	Nonanoic acid, sulfophenyl ester, sodium salt (NOBS)
(4) CAS Number (s)	91125-43-8
II. Modeling Objective	
(5) Modeling Study Objective	Estimate consumer exposure during use in laundry detergent-hand laundering scenario for comparison with P&G calculations.
III. Description of Model	
(6) Tool or Model	E-FAST-US EPA Screening Level Model
(7) Validation/Peer Review	
(8) Availability and Documentation	EPA Website http://www.epa.gov/opptintr/exposure/docs/efast.htm
IV. Description, Inputs and Results	
(9) Description of Modeled Scenario	Consumer dermal exposure to ingredients in granular and tablet laundry detergents can arise from hand laundering of delicate fabrics after dilution in wash water. This study models the external exposure of this scenario.
(10) Exposure Medium Modeled	
(11) Input parameters	EPA's E-FAST model was run using default values in the Liquid Laundry Detergent scenario (model does not contain granule scenario). Parameters included a frequency of 52 times per year, solution concentration of 0.00013 g/cm^3, exposure of both hands and film thickness of 0.005 cm.
(12) Results	1.3×10^{-6} g/kg/day
(13) Reliability	The calculated result is an external exposure estimate. E-FAST assumes 100% dermal penetration. Actual dermal penetration of this substance is less than 1%. The hand laundering task duration is in the range of 5-10 minutes, which is not considered in the calculations. Thus the estimate is very conservative.
(14) Remarks	The purpose of running this model was to compare the results with calculations developed by P&G, which produced a very comparable 7.5×10^{-6} g/kg/day external exposure estimate for this scenario.

Outline C: Modeling Evaluations

I. Identification Information	
(1) Assessment Identification and Date	NOBS—October 2001
(2)Chemical Category	--
(3) Chemical Name (s)	Nonanoic acid, sulfophenyl ester, sodium salt (NOBS)
(4) CAS Number (s)	91125-43-8
II. Modeling Objective	
(5) Modeling Study Objective	Estimate consumer exposure during use in laundry detergent-fabric pretreatment scenario for comparison with P&G calculations.
III. Description of Model	
(6) Tool or Model	E-FAST-US EPA Screening Level Model
(7) Validation/Peer Review	
(8) Availability and Documentation	EPA Website http://www.epa.gov/opptintr/exposure/docs/efast.htm
IV. Description, Inputs and Results	
(9) Description of Modeled Scenario	Consumer exposure to ingredients in granular and tablet laundry detergents can arise from dermal exposure during pretreatment of fabrics, prior to machine washing. This study models the external exposure of this scenario.
(10) Exposure Medium Modeled	
(11) Input parameters	EPA's E-FAST model was run with the user-defined scenario (model does not contain pretreatment scenario). Parameters included a frequency of 365 times per year, solution concentration of 0.033 g/cm^3, exposure to 25% of hands and film thickness of 0.005 cm.
(12) Results	6.6×10^{-4} g/kg/day
(13) Reliability	The calculated result is an external exposure estimate. E-FAST assumes 100% dermal penetration. Actual dermal penetration of this substance is less than 1%. The fabric pretreatment task duration is in the range of 5-10 minutes, which is not considered in the calculations. Thus the estimate is very conservative.
(14) Remarks	The purpose of running this model was to compare the results with calculations developed by P&G that produced a very comparable 4.1×10^{-4} g/kg/day external exposure estimate for this scenario.